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ENTEROVIRUS INFECTIONS IN TORONTO, 1959*

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ENTEROVIRUSES have been found in patients admitted to the Hospital for Sick Children with aseptic meningitis during each summer since 1950.[1, 2] Although occasional cases of aseptic meningitis are encountered during the cooler months, November to June, most have occurred during July, August, September and October, with the peak in late August. Furthermore, the occurrence of enteroviruses in patients with aseptic meningitis and certain other syndromes including pericarditis and pleurodynia is sharply confined to summer and early autumn.

Although the same syndrome, aseptic meningitis, has been encountered each year, the dominant type of enterovirus associated with it has undergone successive changes.[3] Thus Coxsackie B2 virus was the dominant type of enterovirus in Toronto in 1954,[4] but afterwards few infections with the virus were encountered until 1959, when it again became dominant. During the intervening years the principal enteroviruses were ECHO (untyped) in 1955,[5] ECHO 9 in 1956[6] and 1957,[2] and Coxsackie B5 in 1958.[1] Evidence presented below shows that Coxsackie B2 was the dominant enterovirus type in association with aseptic meningitis during 1959.

The diversity of syndromes seen after infection with Coxsackie B5 virus in 1958 in Ontario[3, 7] was in sharp contrast to those after Coxsackie B5 infections in Minnesota[8] and Iowa[9] in 1956, where aseptic meningitis was the only syndrome encountered. However, Gordon *et al.*[10] noted pericarditis and pleurodynia during epidemic spread of Coxsackie B5 virus in northern California in 1956. In Toronto during 1959, although Coxsackie B5 was found in only six patients, two of these presented with pericarditis. In contrast to 1958 when Coxsackie B5 virus exclusively was associated with cases of pleurodynia, several types of enterovirus were isolated from patients with pleurodynia in 1959.

EXPERIMENTAL METHOD

Fæces and cerebrospinal fluid from patients were examined for the presence of enteroviruses by inoculation of tissue cultures of trypsin-dispersed kidney epithelial cells of rhesus monkey, according to methods described previously.[7] Fresh virus isolates were typed using the following standard antisera: Coxsackie A9, B1, B2, B3, B4, B5; ECHO 2,6,9,13,14,16. Serum samples obtained during the acute and convalescent phases of illness were examined for neutralizing antibody to 100 TCD_{50} of various enteroviruses, using two monkey-kidney-culture tubes per fivefold dilution of serum.

RESULTS

Between July 1 and October 31, 1959, 75 children aged seven days to 14 years were admitted to The Hospital for Sick Children with aseptic meningitis. Fæces from 50 of them and a quantity of cerebrospinal fluid from 54 were examined for virus content (Table I). Of the 29 patients who excreted an enterovirus in either cerebrospinal fluid or fæces or both, nine were found to have Coxsackie B2 virus; three, Coxsackie B5; two, Coxsackie A9; two, Coxsackie B4; and one each had Coxsackie B3, ECHO 6, ECHO 9 and ECHO 14 viruses respectively. Enteroviruses isolated from nine patients have not been neutralized by typing sera used routinely, but some of these untyped strains are related antigenically to each other. Thus Coxsackie B2 virus was the dominant serotype associated with aseptic meningitis in southern Ontario during the summer of 1959.

Acute and convalescent phase sera from 21 patients who excreted an enterovirus were tested for neutralizing antibody to prototypes of the same virus strains as were isolated from patients or to the patient's own virus strains. Fivefold or greater increases in the level of homotypic antibody—detected in paired sera of 17 patients—strongly suggest that these viruses caused generalized infection at the time of illness. Furthermore, four patients from whom no virus was isolated had detectable Coxsackie B2 antibody titres in sera

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TABLE I.—VIRUS ISOLATIONS AND ANTIBODY STUDIES IN 75 PATIENTS WITH ASEPTIC MENINGITIS

Virus type	*Virus in fæces*	*Virus in CSF*	*Virus in fæces and/or CSF*	*Homotypic antibody in virus excretions*		
				Rising	*Elevated*	*Total tested*
Coxsackie A9	2	1	2	1	0	1
Coxsackie B2	5	7	9	4	0	5
Coxsackie B3	1	0	1	1	0	1
Coxsackie B4	2	0	2	1	0	1
Coxsackie B5	1	2	3	3	0	3
ECHO 6	0	1	1	1	0	1
ECHO 9	0	1	1	1	0	1
ECHO 14	1	1	1	0	0	1
Untyped	6	6	9	5	0	7
Total positive	18	19	29			
Total tested	50	54	75			

obtained one week or less after onset. The detection of a fivefold or greater increase in Coxsackie B2 antibody levels in all four sera taken two to three weeks subsequently suggests that these patients were infected with Coxsackie B2 virus.

One patient who was maintained on cortisone for treatment of nephrosis developed aseptic meningitis accompanied by weakness of muscles in the right leg and foot. Although Coxsackie B2 virus was isolated both from cerebrospinal fluid and fæces, no Coxsackie B2 antibody was detected in sera obtained at four and 34 days after onset of symptoms. This patient regained almost full muscle power three months later.

TABLE II.—VIRUS ISOLATIONS AND ANTIBODY STUDIES IN 16 PATIENTS WITH PLEURODYNIA

Virus type	*Virus in fæces*	*Rising titre of antibody*
Coxsackie B2	3	3/3
Coxsackie B3	1	not tested
Coxsackie B4	2	2/2
Coxsackie B5	1	not tested
ECHO 2	2	not tested
Untyped	1	not tested
Total positive	10	5
Total tested	16	5

Of the 16 patients who presented with pleurodynia between July and October 1959, 10 excreted an enterovirus in fæces obtained between one and seven days after onset of chest pain (Table II). Coxsackie B2 virus was excreted by three patients, all of whom had rising antibody titres to this virus; and Coxsackie B4 virus was detected in the fæces of two patients, both of whom had rising Coxsackie B4 antibody titres. This shows that these two viruses caused infection in these patients at the time of their respective illnesses. Although ECHO 2 virus was detected in the fæces of two patients, its etiological significance has not been firmly established since acute and convalescent sera from these patients were not available for testing.

Acute benign pericarditis clinically resembling pericarditis due to Coxsackie B5 virus described in 1958[7] was encountered in two patients during 1959. Both patients excreted Coxsackie B5 virus in fæces obtained nine and 12 days after onset respectively (Table III). Rising Coxsackie B5 antibody titres in paired sera from patient V.M. and elevated titres in patient L.W.'s sera are consistent with concurrent infection by this virus. A third patient, R.S., developed a pericardial friction rub two weeks after he first experienced recurrent bouts of colicky abdominal pain accompanied by vomiting. He was afebrile throughout his illness; virus was not isolated from fæces of R.S. and neutralization tests on paired sera have given no suggestion of a possible etiological agent.

Of three children who presented principally with signs of acute myocarditis, an enterovirus (Coxsackie B4) was found in the fæces of one patient only. This patient had elevated Coxsackie B4 antibody titres in sera taken 18 and 22 days after onset of illness.

TABLE III.—VIRUS ISOLATIONS AND ANTIBODY STUDIES IN PERICARDITIS AND MYOCARDITIS

Syndrome	*Patient*	*Age (years)*	*Onset*	*Virus in fæces*		*Antibody titres*			
				Days after onset	*Type*	*Days after onset*	*Coxsackie B2*	*Coxsackie B4*	*Coxsackie B5*
Pericarditis	L.W.	10	29/8/59	12	B5	10	0	0	6250
						16	0	0	6250
	V.M.	12	12/9/59	9	B5	8	10	0	50
						15	10	0	250+
	R.S.	2	26/9/59	17	0	17	0	0	0
						23	0	0	0
Myocarditis	C.S.	12	11/8/59	18	0	16	0	250	0
						28	0	250	0
	H.W.	12	17/8/59	16	B4	18	20	250	0
						22	20	250	0
	D.C.	13	5/10/59	20	0	22	250	20	2500
						29	250+	20	6250

TABLE IV.—VIRUS ISOLATIONS AND ANTIBODY STUDIES IN 22 PATIENTS WITH PARALYTIC POLIOMYELITIS

Poliovirus type	*Virus in fæces*	*Virus in CSF*	*Homotypic antibody response* *Rising titres*	*Elevated titres*	*Total tested*	*Vaccine dosage* *>3*	*<3*
I.	20	0/15*	12	8	20	3	17
II.	1	0/1	1	0	1	0	1
III.	1	0/1	0	1	1	0	1

*Numerator: Number of specimens containing virus.
Denominator: Number of specimens tested.

Between January 1 and October 31, 1959, 22 children were hospitalized with paralytic poliomyelitis. All excreted poliovirus in fæces (Table IV). Although most fæcal samples were obtained less than one week after onset of paralysis, virus was also found in fæces obtained up to 30 days after onset. Viruses isolated from 20 patients were poliovirus type I, one patient excreted type II and a further patient, type III virus. However, virus was not isolated from cerebrospinal fluids obtained from 17 patients between one and four days after onset. During this same period only two cases of non-paralytic poliomyelitis were encountered, i.e. cases who had signs of aseptic meningitis and excreted type I and II viruses respectively.

or shortly after an attack of mumps were admitted to hospital. By inoculation of monkey-kidney cultures with cerebrospinal fluid samples obtained between one and nine days after onset of meningeal signs, mumps virus was isolated from three patients out of 10. Fourfold increases in antihæmagglutinin titre to four agglutinating doses of mumps virus (Enders strain) were detected in paired sera from three patients, one of whom excreted virus. The sera were heated at 56° C. for 30 minutes, and treated with M/100 potassium periodate before testing. Elevated levels of mumps antibody were detected in sera obtained between two and 20 days after onset of meningeal irritation in five patients, one of whom yielded virus in cerebro-

TABLE V.—VIRUS ISOLATIONS AND ANTIBODY STUDIES IN THREE PARALYTIC PATIENTS WHO RECEIVED THREE OR MORE DOSES OF VACCINE

Name	*Age years*	*Onset*	*Virus in fæces* *day*	*type*	*Virus in CSF* *day*	*type*	*Antibody titres* *day*	*I*	*II*	*III*	*Vaccine dosage*
							2	100	250+	250+	
M.B.	4	31/8/59	5	1	1	0	11	2500	250+	250+	4
							3	100	250	0	
N.G.	3	3/9/59	5	1			9	500	250	0	3
							3	20	250	0	
N.F.	4	12/9/59	3	1	2	0	9	500	250+	10	4

Of 20 patients who excreted type I poliovirus, paired sera from 12 showed fivefold or greater increases in neutralizing antibody titre to this virus, and paired sera from a further eight had elevated type I antibody levels in early and late samples. The one patient who excreted type II virus had a fivefold rise in type II antibody titre. The single excretor of poliovirus type III had elevated levels of type III antibody in sera taken five and 12 days after onset.

Although 14 paralytic patients received no injections of trivalent inactivated poliomyelitis vaccine (Salk type) and another five patients received one or two doses, three who excreted type I virus had received three or four doses of Salk vaccine less than six months before onset of paralysis. Results of neutralizing antibody titrations (Table V) were: rising type I antibody titres occurred in all three patients; the levels of type II antibody were elevated in three patients; and two patients had insignificant amounts of type III antibody. Patient N.F., who was severely paralysed in both legs, evidently did not produce antibody until stimulated by injection with living type I poliovirus.

Between July and October 1959, 11 cases of meningoencephalitis that occurred together with spinal fluid. Sera were not obtained from the remaining patient, from whose cerebrospinal fluid mumps virus was isolated.

DISCUSSION

In conformity with the pattern of enterovirus infections in Toronto observed during previous years[3] in which the principal serotype for one year had occurred only rarely in other years, Coxsackie B5 virus, which affected a majority of patients with aseptic meningitis and was the sole virus associated with pericarditis and pleurodynia in 1958, affected only six patients in 1959. However, Coxsackie B2 virus, which was dominant in 1954 and has been encountered only infrequently during intervening years, has again become dominant in association with both aseptic meningitis and pleurodynia in 1959. Nevertheless, Coxsackie B5 virus, not Coxsackie B2, was found in two patients with acute pericarditis in 1959.

Although, during each summer between 1955 and 1959 in Toronto, one enterovirus type has been clearly dominant among the viruses associated with aseptic meningitis, small numbers of other enterovirus types have been encountered each summer except 1956.[1, 2, 5] This situation has also

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been observed in Massachusetts in 1951 and 1954,[11] in Connecticut in 1954 and 1955[12] and Missouri in 1956.[13] However, the dominance of one enterovirus strain was less clear in a study of cases of aseptic meningitis in Ohio during 1956,[14] where Coxsackie B2, B3 and A9 were relatively abundant, and other viruses occurred less frequently. These observations are in sharp contrast to the virtually sole occurrence of ECHO 9 virus in epidemics of aseptic meningitis in England[15-17] and Europe[18] during 1955 and 1956, Toronto in 1956,[6] and Nova Scotia[19] and Minnesota[20] in 1957, or ECHO 4 virus in Iowa[21] and ECHO 6 virus in western New York in 1955,[22] or Coxsackie B5 virus in Minnesota[8] and Iowa[9] in 1956. Unlike experiences in Iowa during 1955,[21] when mixed infections with ECHO 4 and poliovirus type I or III were encountered in four patients, and in Toronto during 1952, where five patients excreted Coxsackie B4 and poliovirus in stools, including two who excreted Coxsackie B4 alone in cerebrospinal fluid,[4] mixtures of other enteroviruses with poliovirus have not been encountered in Toronto more recently.

Although Coxsackie B1, B2, B3 and B4 viruses have been found repeatedly in association with epidemics of pleurodynia during the past decade,[23] only recently has evidence been obtained in favour of an etiological relationship between Coxsackie B5 virus and pleurodynia. Of the 18 patients who were admitted to the Hospital for Sick Children with pleurodynia during the summer of 1958, 16 patients excreted Coxsackie B5 virus in fæces and nine showed rising antibody titres to this virus.[1] During the same summer, Coxsackie B5 virus was isolated from fæces of 20 patients out of 27 residents of a Toronto suburb who developed pleurodynia, and elevated or rising Coxsackie B5 antibody titres in paired sera from seven of these were consistent with recent infection by this virus.[24] During 1959, when Coxsackie B5 virus was encountered relatively infrequently, we observed its association with pleurodynia in one patient only. However, in 1959, with the frequent occurrence of Coxsackie B2 virus, three patients with pleurodynia excreted this virus in fæces, and rising Coxsackie B2 antibody titres in all three strongly suggested an etiological relationship. Outbreaks of pleurodynia due to Coxsackie B2 virus[25, 26] have been recorded less frequently than those due to Coxsackie B1, B3 and B4 viruses.[23, 24]

Concepts of the etiology of acute benign pericarditis have been elucidated during recent years by the demonstration of a frequent association between Coxsackie B viruses and this syndrome. Thus the isolation of Coxsackie B3 virus from fæces and rising Coxsackie B3 antibody titres in paired sera from two patients who had fever, pericardial rub and flattening or inversion of T waves of the electrocardiographic leads V_3 and V_4[27, 28] strongly suggested that this virus caused the illness in both patients. An elevated titre of Coxsackie B4 complement-fixing antibody in serum taken from a patient 15 days after onset of acute pericarditis suggested this type of virus as a possible etiological agent.[29] Falling titres of Coxsackie B5 complement-fixing antibody in sera obtained seven weeks and six months after onset of pericarditis suggested the possibility of this virus as the etiological agent in one patient.[30] During epidemic spread of Coxsackie B5 virus in Shasta County, California, in the summer of 1956, seven cases of pericarditis had elevated Coxsackie B5 complement-fixing antibody titres in convalescent sera, and virus was isolated from fæces of one patient who later showed a rising Coxsackie B5 antibody titre.[10] This strongly suggests an etiological relationship between Coxsackie B5 virus and acute pericarditis. In 1958, isolation of Coxsackie B5 virus from five patients with acute pericarditis out of eight patients studied in Toronto, together with the presence of elevated or rising Coxsackie B5 neutralizing antibody titres, pointed firmly to an etiological association between this virus and pericarditis.[1, 3, 7] Further confirmation of this association was obtained in Halifax[31] and Florida[32] by virus isolation and antibody studies in servicemen who developed pericarditis. Isolation of Coxsackie B5 virus from fæces of two patients with pericarditis in 1959, and demonstration of rising homotypic antibody titres strengthened the evidence of an association between this virus and acute benign pericarditis.

SUMMARY

In Toronto, between July and October 1959, enteroviruses were isolated from fæces and/or cerebrospinal fluid in 29 of 75 children who developed aseptic meningitis. The principal enterovirus associated with aseptic meningitis was Coxsackie B2. Coxsackie B2 or Coxsackie B4 viruses were found in association with pleurodynia in five patients out of 16 studied. Coxsackie B5 virus occurred in association with acute pericarditis in two patients of three studied.

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RÉSUMÉ

Les entéro-virus sont incriminés chaque année surtout de juillet à octobre dans un certain nombre de méningites aseptiques de l'enfance. On a observé un changement dans la prédominance des différents types d'une année à l'autres à l'Hôpital des Enfants Malades de Toronto. Ainsi, en 1954, le virus Coxsackie B2 dominait la scène et après une éclipse, il la reprit en 1959. Dans l'intervale, un virus ECHO (non typé) tint la vedette en 1955; en 1956 et 1957, un virus ECHO 9 et, en 1958, ce fut un autre virus Coxsackie B5. On a cherché à identifier les virus en cause dans ces infections tant dans le liquide céphalo-rachidien que dans les selles des jeunes malades atteints; un entéro-virus fut isolé du L.C.R. dans 24 cas et des selles dans 50 cas chez 54 malades. Les épreuves sérologiques pratiquées chez 21 malades ont été positives dans 17 cas. Quatre autres malades de qui on ne put isoler de virus n'en ont cependant pas moins vu leur taux d'anticorps quintuplé. On a aussi observé le contraire (virus isolé sans formation d'anticorps) chez un autre malade recevant de la cortisone pour néphrose. Dans 16 cas de pleurodynie, un virus Coxsackie B2 ou B4 fut isolé chez cinq malades. Deux des trois malades atteints de péricardite aiguë ont passé du virus Coxsackie B5 dans leurs selles, alors qu'un des trois cas de myocardite aiguë semble avoir été causé par un autre de type B4. Les 22 enfants traités pour paralysie poliomyélitique entre janvier et octobre 1959 ont tous excrété des virus de polio dans leurs selles (20 de type I, un de type II et un autre de type III).

THE CLINICAL SIGNIFICANCE OF TIREDNESS

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"It is the very essence of a whole that, while it is formed of its parts, it in turn influences the parts and affects their relations and functions. This reciprocal influence underlies the internality or interior character of a whole."

—J. C. SMUTS[1]

DEFINITION

TIREDNESS is a symptom rather than a clinical condition: its definition is nebulous and as a symptom it must mean different things to different people, both when experiencing and interpreting it. Thus the fatigue of a piece of striated muscle can be measured objectively in the laboratory, and the experiment repeated to confirm previous readings. The fatigue of forearm and hand muscles is measurable, using electronic methods or the dynamometer, but here, other factors may operate, influencing the muscles from above, and may vary independently of the muscles under test, and so modify their ability to tire. Therefore, the impossibility of applying the physical measurement of energy to the descriptive term "tiredness" must be recognized, whether this tiredness is of physical or psychogenic origin.

Tiredness is a "whole" symptom. It is felt throughout the patient's body and is not confined to regions, anatomic structures or specific physiological functions, but rather it emanates from the natural whole of the human body and mind. It is the interrelationship of these two that governs the consciousness of tiredness. That each may have a significant effect upon the other is seen from the following, if rather crude, illustration. When in a decompression chamber, the respirable atmosphere is reduced to conditions found at 25,000 feet, the performance of simple tests, such as dropping peas down a hole, becomes increasingly laborious and at the same time, ludicrous, to both observers and the subject. The latter knows what he wants to do, but is quite unable to perform, showing all the signs of fatigue, in this case due to the effects of anoxia. Again, we are all familiar with the small child who, after a day of considerable activity, exhibits the mental and physical signs of tiredness, irritability and fidgetiness, and who yet may suddenly recover full energy if certain suggestions are made to him which are acceptable and imply that he will benefit in some way, usually through the gastro-intestinal tract!

Most authors agree that the major role is played by the psychological condition of the patient. This is apparent to anyone who has practised medicine in both the northern temperate climates and tropical zones: in the latter, despite poor nutrition and chronic parasitic disease, to name but two prevalent conditions, the complaint of tiredness as a major symptom is seldom made. In temperate-zone practice, it assumes an almost unrivalled position in the patient's list of complaints. We are well aware that the stresses of our way of life act primarily upon the psyche.

The interpretation of a patient's complaint of tiredness requires a degree of patience in history-taking that is often impossible to achieve in practice, so that as an isolated symptom, tiredness often precedes by a significant period the other more recognizable and better understood complaints and findings that occur in both mental and physical disease, such as depression in the former and shortness of breath, pallor and peripheral œdema in the latter.

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PRESENT INVESTIGATION

It has seemed useful to review the case reports of nearly 1200 consecutive patients attending the writer's office. These comprise a series of patients from whom were selected those complaining of tiredness, as either a primary or a major secondary symptom.

The symptom of tiredness can be extracted from almost every patient who attends a doctor because of supposed or real ill-health and its value as a significant symptom is thereby lessened. The art of history-taking demands that suggestion should play a minimal part in obtaining the patient's story, but this is often difficult to avoid: nevertheless, its value as an early symptom is very real and in no place is this more true than in the doctor's office. The cases which have been reviewed were all referred by colleagues and thus these patients tended to be seen when their condition was more advanced. It will be appreciated that the process of history-taking was assisted by the act of consultation and the retrospective view of the patient's progress since his first approach to his physician.

The clinical significance of any symptom is the knowledge that can be obtained and applied from that symptom: tiredness is so broad a descriptive symptom that to be of clinical value it must be related to the essential bodily or mental function that is primarily at fault, and thus we come to appreciate that it is the accompanying, more specific symptoms, which are so important, together with variations of the tiredness itself as modified by the disordered function of the bodily systems: this can be quickly illustrated by the examples of hypoglycæmia and severe anæmia.

CAUSES OF TIREDNESS

Psychogenic

In North American practice, neuro-psychiatric disturbances appear to constitute a major cause of tiredness and are seen as anxiety states, temporary reactive depressions or minor obsessional states, which cause severe emotional disturbance in sensitive patients. From the accompanying tables, it will be appreciated that anxiety states on account of their prevalence have first to be excluded in defining a patient's illness. In the busy day of office practice, the tendency to place many patients in this category has to be constantly appreciated by the doctor.

To explain the mechanism of tiredness in these people is not at present possible on anything but general lines, although it is becoming increasingly recognized that the endocrine system, in particular, plays a part, probably via the influence of the hypothalamus, and that disordered metabolism—for example, in the utilization of carbohydrates and amino acids in respect of enzyme systems—may be of major importance.

The stress of modern life has come to be regarded as a major cause of fatigue: frustration at work; the increasing difficulty of commuting, particularly in the newer rapidly expanding cities; an unbalanced high-carbohydrate diet; excessive tobacco consumption; and alcohol, which at first is often taken to stave off tiredness, but soon becomes a craving. These add up to what we regard as the stresses of life, and contribute to the patient's complaints.

Inquiry into the relationship of tiredness to the environment is of cardinal importance in differentiating so-called functional from organic disease. The knowledge of the onset, quality, quantitative subjective estimation, relieving factors (such as its disappearance at week-ends) of tiredness and its relation to food, certain weather and emotional crises—all of these have to be explored in defining the natural history of the patient's condition.

Not only the medical history, but a very personal occupational and environmental history must be obtained so that the major symptom of tiredness may be viewed objectively. If all the possible avenues are explored—bearing in mind that neurotic tiredness can develop as easily from boredom as from emotion of one sort or another—then its significance in a particular patient becomes clearer, provided organic disease can be excluded.

Endocrine Dysfunction

It is found from experience that sufferers from major endocrine dysfunction have tiredness as a major complaint and usually early in their disease, be it diabetes mellitus, myxœdema, Addison's disease or other more uncommon conditions. Perhaps with regard to the more nebulous effects of dysfunction, the thymus gland in relation to myasthenia gravis may be cited. Undoubtedly a great deal more has yet to be learned of the internal secretions; the examples of primary and secondary aldosteronism and of excessive serotonin secretion from argentaffin tissue spring immediately to mind.

To confuse the relationship of tiredness to endocrine disease further, tiredness may arise as a result of either over-action or under-action of a gland, as exemplified by myxœdema and toxic goitre, diabetes mellitus and hyperinsulinism, Addison's disease and primary aldosteronism, in each of which tiredness may be a major symptom. Its mode of production probably differs in each, variously involving cell respiration, enzymatic processes, electrolyte exchanges and circulatory disturbances.

The undoubted secret of many an apparently smart diagnosis is that the physician has been aware of its possibility, even before reaching the stage of physical examination, and by inference this means that the assessment of the history, in all its aspects, has given the clue to which direction he has to look. This is particularly true of endocrine disease. Since the end-organ involvement frequently differs, the related dysfunctions will be illustrated.

Adrenal.—1. Chronic adrenal cortical deficiency produces a fall in plasma sodium level, owing to decreased reabsorption by the renal tubules. On the other hand, the plasma potassium level increases because of increased reabsorption. These changes in turn lead, probably by reduced circulatory effects, to impaired absorption of carbohyrate and fats and reduction of kidney function and ultimately decreased excretion of nitrogenous metabolites.

2. Specific over-action of the adrenal cortex, as in primary aldosteronism, is manifested by increased excretion of salt-retaining hormone in the urine, increased excretion of potassium, hypertension, muscular weakness and general lassitude; all are manifestations of hypersecretion of adrenal mineralocorticoids.

Pancreas.—3. Diabetes mellitus is primarily due to an absence of sufficient quantities of insulin. This interferes with (1) normal phosphorylation and thus the availability of glucose to the cells, and results in (2) reduction of glycogen formation in the liver and in muscles; (3) failure of conversion of glucose to fatty acids and fat; and (4) an increase in gluconeogenesis, which causes muscle wasting and weakness.

4. Hyperinsulinism can be assessed as a functional or an organic effect. The secretion of insulin is under the influence of the vagus nerves and also the circulating blood glucose. Stimulation of the former lowers blood glucose, and the cerebral centres also influence insulin secretion via the vagi. Rapid increases of blood glucose also cause surging of insulin secretion and a pendulum over-swing is sometimes found in the obese over-eaters. Insulin-secreting tumours, however, are not under nervous or humoral control.

Thyroid.—5. Myxœdema, whether primary or secondary, results entirely from reduction of secretion of thyroxine, the end-product of complicated synthesis in the gland. There is reduced metabolism of all cells and reduced oxygen consumption from the failure of oxidation processes dependent upon enzyme systems. Secondary effects are the interference with carbohydrate absorption and utilization. Thus the nutrition of cells, in particular the nervous system, liver and myocardium, is affected.

6. Thyrotoxicosis causes a rapid increase in metabolism, increased utilization of food and endogenous sources of carbohydrate, protein and fat, and ultimate exhaustion of cells. This results in circulatory failure, vitamin lack and potential exhaustion of insulin-secreting cells in the pancreas, leading to diminished carbohydrate tolerance.

The protean character of these disorders, which are marked by tiredness as a major symptom, points to the numerous end-organ derangements involved. Before leaving the endocrine system, there are two uncommon conditions that the physician may recognize early if he is aware of them. Hyperparathyroidism, due either to primary hyperplasia or to functioning adenoma, is a rare condition but its recognition and treatment can give lasting relief. This syndrome should always be considered in recurrent renal calculi, since they may be caused by excessive renal excretion of calcium. A recent survey of a group of 50 patients with repeated renal calculi revealed that seven subsequently had parathyroid tumours removed—an incidence of 14%.[2] One of the earliest clinical effects of this condition is tiredness, often associated with constipation, and the syndrome should be considered in cases not explained on some other basis. The symptoms may be acute or chronic in onset or the acute phase may complicate the chronic. The end-organs are the muscle fibre (particularly the myocardium) and the nerve fibre, which become increasingly sluggish in action and excitability respectively. Since Weigert[3] first described the association between the thymus gland and myasthenia gravis, the interrelationship of the thymus gland with the other endocrine glands has been demonstrated, in particular with regard to the muscular weakness occurring in thyrotoxicosis and Addison's disease, in both of which hyperplasia of the thymus occurs. With these examples of thymic dysfunction, despite the absence of proof of endocrine secretion, disorders of the thymus gland must be considered in the discussion of muscle weakness and more general tiredness, for which a more obvious cause cannot be found.

A large proportion of women complaining of tiredness fall within the menopausal years, and the natural and frequent assumption made is that tiredness occurs *pari passu* with the menopause and all that is therein implied. The fact that many women have no symptoms whatever during the years accompanying diminishing ovulation is often overlooked, particularly by the laity. Herein lies an ever-present danger: for more serious disease may well be disregarded if the symptoms are ascribed to the "change of life".

The endocrine modification occurring at the menopause is one of sudden or gradual cessation of ovulation and œstrogen secretion, with paradoxical increases of follicle-stimulating gonadotrophic hormone from the pituitary, owing to the release of inhibition once the levels of œstrogen are decreased. Essentially, then, the balance of endocrine secretion is disturbed, and recognizable symptoms accompany the change, such as hot flushes, palpitations, tiredness and irritability, paræsthesiæ of limbs and arthralgia being among the more frequent.

The clinical significance of tiredness within the over-all framework of the menopause picture is therefore not large by itself and must be viewed in conjunction with the whole. As a rule it is not a major symptom unless there is some more obvious cause such as secondary anæmia from excessive bleeding, loss of sleep from nocturnal cramps or arthralgia, insufficient food intake related to psychogenic anorexia, and indeed other syndromes occurring within the menopausal picture.

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Metabolic Abnormalities

Many examples of metabolic disorders causing tiredness can be cited, ranging from long-recognized latent uræmia due to a variety of conditions to the classical syndromes of sodium deficiency in heat exhaustion and potassium derangement after prolonged surgery or loss of intestinal secretions.

Metabolism, by definition, embraces all the physical and biochemical agencies whereby the body cells derive energy and material to replace that expended, and thus covers disorders of kidney, liver, blood, electrolyte, water and vitamin metabolism, which are the chief actors and interactors in tissue exhaustion and breakdown, and the precursors of clinical tiredness.

Kidney.—The chief function of the kidney is to remove from the body waste and other undesirable substances and whatever water and solid material may have been formed in or introduced into the body in excess of the quantity required. Renal dysfunction may develop from either local renal disease or the effects upon the kidney of systemic disorders, affecting primarily the circulation and protein metabolism. Depression of the former by reducing the glomerular filtration rate and tubular reabsorption causes nitrogen retention and electrolyte and water disorders, the secondary effects of pituitary antidiuretic hormone and adrenal aldosterone being now considered of some importance. The secondary effects of increased protein breakdown due to infection and dehydration add to the retention of nitrogenous products. Nephritis itself, while primarily affecting the glomeruli and vascular tree in glomerulonephritis and the tubules in pyelonephritis, initially or eventually leads to nitrogen retention, together with profound effects on the acid-base balance and water metabolism of the body. It is, however, the chronic disease, whether pre-renal or renal, and its slow insidious effects with which we are concerned.

The activity of the individual cell is related to the depolarization across the cell membrane, which is accompanied and possibly provoked by passage of the potassium ion in a similar direction. Any significant disturbance of potassium, and also calcium and magnesium, which are closely related to potassium in its action on cells, will profoundly affect the function of these cells. The relationship of such electrolyte changes to clinical tiredness must remain, for the time being, theoretical, but should, notwithstanding, be considered in any patient presenting with significant tiredness.

Liver.—Disorders of this organ, which are in the present series essentially cirrhosis and infectious hepatitis, accounted for 11.4% of all cases and constituted the second largest group. Complex functions of the liver involving protein, fat and carbohydrate metabolism, pigment metabolism, enzyme systems, vitamin production or storage, detoxication and excretion cover all the vital functions of the body to some extent. Added to this, the parenchymal liver cells are among the most sensitive in the body to changes in their environment brought about by lowered oxygen tension and toxic agents. Undoubtedly many of the common disorders of the body cause debility and symptoms of tiredness through depression of liver-cell activity. Today we have more scientific evidence of why and how this occurs, but our predecessors certainly recognized the significance of these disorders. The bile has long been recognized as one of the most important humors of the body and with good reason, for, as biochemistry continues to reveal, the bile is concerned in many disorders extending beyond the borders of the liver and involving removal of toxic products, pigment derangements and enzyme activity.

Many tests of liver function are used today and certainly the common observation of co-relation of abnormal liver function tests and physical tiredness is frequently made, mostly, it must be admitted, in the convalescent period following an occult or overt attack of hepatitis from one cause or another. The significance of such abnormal tests is difficult to assess, for they may remain abnormal long after the patient claims full recovery. Nevertheless, it is wise to bear in mind the relation of liver disorder to other body systems, in particular the endocrine, with emphasis on the thyroid gland and the male and female sex hormones.

Liver functions embrace a wide field and we can touch upon only a few that have a direct bearing upon cell nutrition and clinical tiredness. The former, by definition, includes the metabolism of carbohydrate and fat, the chief sources of energy, and of protein from which is derived the source for tissue replacement.

The liver is the great store-house of carbohydrate and, to a lesser extent, of fat, the carbohydrate being laid down as glycogen and the fat as fatty acids in the normal organism, although in disease, neutral fat or cholesterol esters may accumulate, and glycogen may have to be replaced either because of intrinsic liver disease or because of systemic disorders. The relationship of tiredness to carbohydrate is close and is brought about by the influence of circulating insulin, which controls the direction in which the products of carbohydrate metabolism flow, i.e. into the liver or into the muscle or brain cell, and also the ability of those cells to use those products. A recent article[4] has called attention to the profound effect of a reduced circulating blood sugar level upon the psyche, particularly that of releasing mild neurotic manifestations such as tension, weakness, tiredness, anxiety, irritability and restlessness. This may represent a major part of the problem of tiredness in general and certainly bridges the gap between the mind and the body mentioned earlier. Mobilization of liver glycogen is also under the influence of adrenaline, which again illustrates that psychological stimuli may relieve tiredness by organic means.

On the other hand, accumulation of fat in the liver appears to be a consequence rather than a cause of many disorders, and the relationship of tiredness to deranged fat metabolism in these cases is probably illusory.

The cause of the bizarre group of conditions collectively known as "periodic paralysis" has been shown to be related to the level of potassium in the serum, which is diminished during an attack. The phenomenon has been noted to be related to meals, particularly those with high carbohydrate content. This suggests a relationship between potassium and carbohydrate, which is indeed the case, the former moving with the latter into the liver, in addition to the shift of potassium from the extracellular to the intracellular space.

In patients with cirrhosis, glycogen storage is impaired and the body's supply of rapidly available carbohydrate diminished. Whether there is deficient storage or availability of potassium is a question, but if this was the case, the gross muscular asthenia and tremor might be explained.

Electrolytes

In describing the effects of kidney and liver dysfunction, we touched upon the role of potassium in relation to cell activity. This role illustrated that the metabolic effects of electrolytes are closely bound up with the major functional systems and any resultant effects from electrolyte derangement are inevitably due to some systemic abnormality, except in those cases where the effects are due to inadequate or excessive ingestion of electrolytes.

The chief cations responsible for normal metabolism are sodium, potassium, calcium and magnesium, and the anions are chloride, bicarbonate and phosphates. The cell, which contains mainly potassium and phosphate and a small amount of magnesium within it, is bathed in a fluid rich in sodium, calcium, chloride and bicarbonate. There is a constant dynamic equilibrium, that is, a passage of electrolytes within and without the cells and continual modification of the intra- and extracellular fluid, and it is this dynamic equilibrium which may be called the "spark of life". Nevertheless, the cell is primarily dependent upon potassium, which appears to control its excitability, or response to stimulus, as well as influence the permeability of the cell membrane. The cation calcium shares with potassium this excitatory and, in high concentration, inhibitory action on cells, seen clinically most clearly by their effect on the myocardium in the electrocardiogram. In hyperkalæmia from any cause (to give examples, adrenal cortical failure and chronic renal disease), great muscular asthenia and depression of cell sensitivity are well-recognized phenomena, and although these are not attributed solely to changes in potassium ion concentration, they have a distinct clinical relationship.

The case of magnesium, however, is far from clear, and has only recently emerged as one of possible clinical significance. Magnesium is present in both red blood cells and plasma and has a reciprocal relationship to calcium, but the knowledge of its utilization is still imperfect, although an increase in magnesium in the serum of patients with chronic glomerulonephritis has been repeatedly confirmed. The phenomena found in magnesium intoxication have long been known; they form the basis of the clinical use of magnesium for its sedative effect, both general and local, on the muscular system, including the myocardium. Muscular weakness, sleepiness and coma resemble symptoms seen in uræmia: a possible relationship is suggested.

Blood

Discussion will be limited to the effects of diminished oxygen carriage, the essential for adequate function being the concentration of hæmoglobin in the red blood cells and the total quantity of circulating red blood cells. The utilization of oxygen by tissues is continuous, but certain factors may modify the rate of utilization, such as endocrine influence on the rate of cell metabolism which is well recognized, the slow rate seen in hypothyroid function exemplifying this. It is beyond the scope of this paper to elaborate upon oxygen utilization and interchange by the tissues, but necessary to appreciate their significance. A recent article[5] has emphasized the importance of recognizing that interference with oxygen carriage may be more common than is realized: the author described 41 cases of chronic carbon-monoxide poisoning with presenting symptoms of headache, anorexia, dyspepsia, weakness and dizziness—all too common complaints in a doctor's office.

The total quantity of circulating red blood cells determines the availability of oxygen to the tissues, and any reduction leads to deprivation of the tissue cells and the symptoms and consequences of anæmia. This reduction may occur from any of the conditions which interfere with adequate erythrocyte formation, by increasing their rate of destruction or causing excessive loss. There is no doubt that oxygen lack is the first cause of tissue cell exhaustion, which is manifested early by clinical tiredness.

A third cause of impaired utilization of oxygen by tissue cells is not directly concerned with the blood elements themselves, but rather the exchange of gases across the pulmonary membrane. This impaired utilization may arise from obstruction anywhere along the upper or lower respiratory tract, from an inadequate airway due to enlarged adenoids and tonsils to a reduction in total pulmonary epithelium in severe emphysema. The former may manifest itself as tiredness and listlessness in children and may be overlooked unless kept in mind.

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Chronic infection and infestation, long recognized as potent causes of tiredness, act mainly through their harmful influence on the blood-forming tissues in the marrow and by chronic blood loss through the gastro-intestinal and genito-urinary tracts.

Malignant Growths

The distinction of malignant from benign growths is made clinically on the basis of the resultant effect of the tumour. The modern concept of the chemical nature of the metabolic abnormality of malignant tumours is gaining ground: this metabolism differs from that of ordinary cells to such an extent that essential nutrients are used up at a much faster rate and available supplies are rapidly exhausted. This plays a part in the symptomatology of the patient and may explain the vague symptoms of tiredness and disordered function often found before a tumour has begun to exert its effects by size, blood loss or necrosis.

RESULTS OF INVESTIGATION

Out of a total of 1170 cases seen, 105 complained of tiredness, lassitude or exhaustion as either primary or major secondary symptoms: this is an incidence of 8.9%, which is perhaps somewhat lower than expected, although it does represent only those patients who spontaneously complained of tiredness, rather than those in whom tiredness could be revealed by questioning and suggestion. Of the 1170 cases surveyed, the largest group were cardio-vascular, with the combined group of chronic or acute anxiety state and tension running second (see Table I). The high rate of the latter group in this series may be explained on two counts: firstly, many of the problems of diagnosis are referred from their family doctors and, thus, many so-called functional cases are channelled to this office and secondly, to support this, these patients are gathered from a suburban area approximating a large and busy commercial city, and many of them are exposed to the stresses of competitive business life with the additional fatigue of commuting daily.

TABLE I.—INCIDENCE OF TIREDNESS AMONG THAT GROUP OF DISEASES IN WHICH IT OCCURS AS A MAJOR COMPLAINT, OUT OF A TOTAL OF 1170 CASES REVIEWED

Order of frequency	*Disease*	*Number of cases*	*Per cent*	*Number of cases of tiredness in each group*	*Per cent*
1	Hypothyroidism	6	0.5	3	50.0
2	Anæmia	14	1.2	6	42.1
3	Liver disease	23	2.0	9	39.1
4	Infectious mononucleosis	16	1.3	6	37.5
5	Hyperthyroidism	14	1.2	5	35.7
6	Anxiety or tension states	104	8.8	26	25.0
7	Duodenal ulcer	22	1.8	4	18.1
8	Diabetes mellitus	28	2.4	4	14.3
9	Heart disease	166	14.2	9	5.4

Of the 105 cases of tiredness which have been further analyzed, the largest group was anxiety-tension, heart disease and liver disorder being each a long way behind (see Table II). However, a breakdown of actual cases in each major diagnostic group reveals some possibly significant information, which, in view of the relative paucity of cases, however, will not stand statistical evaluation. Thyroid deficiency, of which there were six cases, was the group with the highest incidence of tiredness; anæmia was a close second, followed by liver disease, infectious mononucleosis and thyrotoxicosis. The anxiety-tension cases were a considerable distance behind and this, I believe, emphasizes the significance of tiredness as a major symptom of primarily physical disease. Of the 14 cases of anæmia in the total series of 1170 there appears to be an equal distribution of iron deficiency and secondary anæmia, with the occasional case of pernicious anæmia and hæmolytic anæmia. In the 6% complaining primarily of tiredness this distribution was again found, and no one type predominated. From a survey of this nature, it appears that tiredness is principally a symptom of organ disease and that due emphasis must be placed upon this symptom, when spontaneously offered, with particular reference to endocrine, blood, and liver diseases, and chronic infections.

TABLE II.—BREAKDOWN OF 105 CASES PRIMARILY COMPLAINING OF TIREDNESS

Diagnosis	*Number of cases (105)*	*Expressed as percentage*
Alcoholic gastritis	1	0.95
Anæmia	6	5.7
Aneurysm of aorta	1	0.95
Anxiety state or tension	26	24.75
Carcinoma of colon	2	1.9
Carcinoma of lung	2	1.9
Cerebrovascular disease	1	0.95
Cholecystitis	2	1.9
Cirrhosis and hepatitis	9	8.5
Dental infection	1	0.95
Depression states	2	1.9
Diabetes mellitus	4	3.8
Duodenal ulcer	4	3.8
Encephalitis	1	0.95
Goitre	1	0.95
Heart disease	9	8.5
Hypertension	1	0.95
Hypoglycæmia	1	0.95
Hypothyroidism	3	2.85
Ileitis	1	0.95
Influenza	2	1.9
Labyrinthitis	1	0.95
Leukæmia	1	0.95
Malaria	1	0.95
Infectious mononucleosis	6	5.7
Nephritis	2	1.9
Obesity	2	1.9
Overwork	2	1.9
Pneumonia	1	0.95
Pregnancy	2	1.9
Pyrexia of unknown origin	1	0.95
Sinusitis	1	0.95
Thyrotoxicosis	5	4.75

CONCLUSIONS

The explanation given for the probable causes of tiredness embraces and attempts to integrate most of the essential bodily and mental processes. It would seem that tiredness results from impairment of this integration and this obtains some

support from the observations of Gould[6] concerning the impairment of resources and of cerebral metabolism in infectious illnesses, which lead to imperfect psychiatric integration, finally resulting in post-infective debility.

Analysis of the present series reveals clearly the predominance of physical disorders in patients with significant tiredness; also, that such a complaint often heralds serious, but not necessarily irreversible, disease. Herein lies the practical application of this study, namely, that when a spontaneous complaint of tiredness, lassitude, lack of drive or exhaustion is made, careful inquiry and examination must be undertaken before consigning the case to what has been described as the clinical rubbish basket of neurotic ill-health.

SUMMARY

A survey of nearly 1200 consecutive cases of varied medical disorders has been made and 105 extracted in which the primary complaint was of tiredness. These have been analyzed and the relation of tiredness to specific conditions defined, particularly the predominance of tiredness as a symptom of physical rather than neurotic disorder. An attempt has been made to integrate the physiological and psychological processes which may take part in the production of this symptom, with particular reference to disorders of the endocrine, genito-urinary and hæmopoietic systems in relation to specific processes of metabolism.

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RÉSUMÉ

La fatigue est plutôt un symptôme qu'une entité clinique. Dans certains cas elle peut être mesurée objectivement mais dans d'autres il faut se fier à la description subjective du malade. La plupart des auteurs s'accordent pour déclarer que sa cause principale dépend de l'état psychologique du sujet. Afin de déterminer le rôle que joue la fatigue dans la symptomatologie des cas de médecine courante, l'auteur a revu 1200 dossiers de malades qui se sont présentés à son cabinet de consultation accusant de la fatigue comme symptôme primaire ou secondaire. La fatigue causée par l'état d'angoisse se rencontre assez fréquemment de nos jours et ne peut être déterminée qu'à l'aide d'une anamnèse détaillée. La plupart des troubles endocriniens peuvent causer de la fatigue. L'auteur cite en exemple le diabète, le myxœdème, la maladie d'Addison, la myasthénie grave et la ménopause. On peut aussi impliquer les troubles du métabolisme qui se manifestent par de l'urémie, des pertes de sodium ou de potassium, un manque de vitamines ou un déséquilibre de l'eau et des électrolytes. Les affections rénales et hépatiques sont souvent en cause dans ces cas. L'anémie peut également engendrer de la fatigue par l'apport inadéquat d'oxygène aux tissus. Il convient d'ajouter que si les tissus ne sont pas en mesure d'employer l'oxygène ou si l'échange gazeux au niveau des alvéoles pulmonaires ne peut s'effectuer de façon satisfaisante le résultat est le même quel que soit le degré d'hémoglobine. Parmi les autres causes de fatigue, notons les néoplasmes et certaines infections chroniques.

ANKYLOSING SPONDYLITIS*

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DEFINITION AND ETIOLOGY

ANKYLOSING SPONDYLITIS is an inflammatory disorder of unknown etiology that involves not only the sacro-iliac and apophyseal joints of the spine, but also bony surfaces at sites of ligamentous, fascial or muscular attachments; synchondroses such as the manubrio-sternum, xiphi-sternum, symphysis pubis and intervertebral discs; frequently the costo-vertebral articulations, and at times, one or more extra-spinal or peripheral joints. Some degree of ankylosis of the affected joints, and calcification or ossification in the annulus fibrosus of intervertebral discs and in paravertebral tissues and ligaments, are commonly but not invariably present.

The relationship of ankylosing spondylitis to rheumatoid arthritis remains to be clarified but the weight of evidence at present favours the concept that these two diseases are separate entities. The striking predominance among males; the consistently negative tests for serum rheumatoid factor; and the absence of that rheumatoid hallmark, the connective tissue necrobiotic nodule, in patients with ankylosing spondylitis are among the more impressive of the many fundamental differences between this disease and rheumatoid arthritis.[1]

Ankylosing spondylitis begins characteristically in early adult life, between the ages of 18 and 35 years in 85% of patients. Males are affected nine to ten times as frequently as females.

ONSET

The onset is gradual and insidious in two-thirds of cases and more acute and abrupt in the remainder. In the majority, the earliest symptoms are referred to the low-back area but in 15 to 20% the disease begins as an acute inflammatory arthritis of one or more of the peripheral joints. Rarely, the initial pain and stiffness have a diffuse non-articular distribution in the thorax, the neck, or throughout the limbs.

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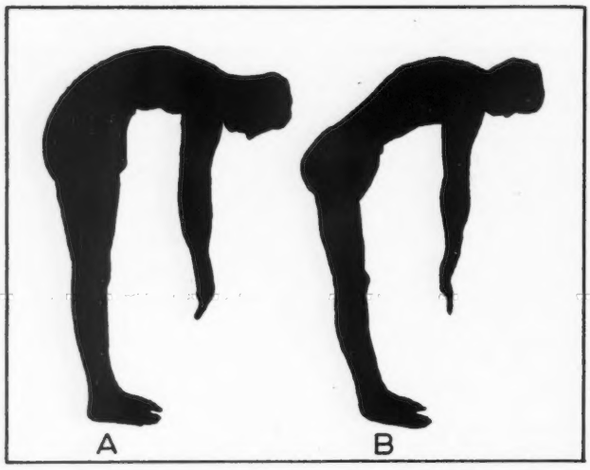

Fig. 1.—Silhouettes of (A) normal individual and (B) patient with ankylosing spondylitis, reaching toward the toes without flexing the knees. Note flattening and loss of flexibility of lower thoracic and lumbar spine of the spondylitic in contrast to the normal uniformly regular spinal curve.

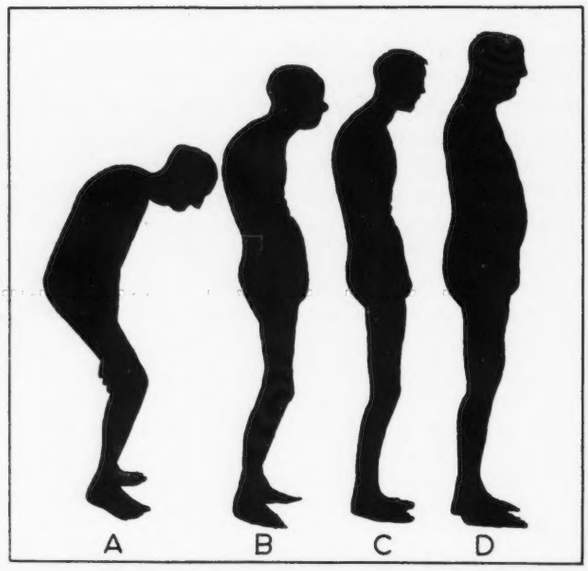

Fig. 2.—Silhouettes of four patients with ankylosing spondylitis illustrating varying degrees of static postural deformity. Note the forward thrust of head and neck, depression of chin toward the chest, the flattened "ironed-out" lumbar curve, upward tilt of pelvis and semi-flexion of hips and knees. Patient A illustrates severe degree of these abnormalities, while patient D has maintained almost normal posture.

SYMPTOMS

The usual complaint is dull aching pain located in the low-back region in the early stages but tending to spread proximally up the spine as the disease progresses. As a rule the back pain is accompanied by a subjective sense of stiffness, often aggravated by cold, dampness, physical inactivity, or strenuous exertion and relieved temporarily by heat, salicylates and mild "limbering-up" exercise. Morning stiffness and "jelling" are common. Sharp stabbing pain may occur spontaneously but is brought on more often by sudden movements, jarring, coughing, sneezing or straining. Many patients describe a vague sense of weakness, tiredness and instability in the musculature of the affected regions. "Girdle-pain", a tight band-like feeling of constriction around the chest or abdomen, is a frequent complaint. In the presence of active arthritis of the cervical spine, pain may spread up the neck to the occiput and around the temporal, parietal and frontal areas of the cranium, resulting in severe headaches, spasmodic in occurrence but steady and non-throbbing in character, usually aggravated by sudden neck movements. Radiation of low back pain into the buttocks and thighs is a common symptom which may bear a superficial resemblance to sciatic pain due to herniation of an intervertebral disc or other lesion causing sciatic root compression. It differs from the latter, however, in that it usually varies from one side to the other, rarely extends below knee level, and is not accompanied by sensory, motor or reflex changes. Fatigue is often a prominent symptom and may be accompanied by loss of weight, malaise and general weakness in its more severe form.

PHYSICAL SIGNS

Occasionally, in the early stages of the disease, there may be no abnormal findings on physical examination. In the great majority, however, there is some reduction in spinal mobility, particularly in the lumbar region which characteristically reveals decreased flexibility and flattening when the patient attempts to stoop forward and reach toward his toes without flexing the knees (Fig. 1). In later stages of the disease, cervical mobility may also be reduced and in advanced cases the entire spine from occiput to sacrum may be ankylosed and rigid.

The typical postural abnormalities include a flattening and "ironing-out" of the lumbar curve, a smooth, rounded, thoracic kyphosis, forward protrusion of the head and neck with depression of the chin toward the chest, and less commonly, scoliosis. The pelvis may be tilted upward and the hips and knees semi-flexed, the over-all effect of these postural abnormalities producing a "simian" or ape-like posture. The extent and severity of deformity varies greatly from patient to patient (Fig. 2).

Decreased costovertebral movement and reduced chest expansion are frequently observed.

Spinal and sacro-iliac tenderness may be present during active stages of the disease, and spasm and atrophy of the paravertebral, abdominal, gluteal and thigh muscles are not uncommon.

Reduction in the range of hip and shoulder movement is demonstrable in about one-quarter of patients.

In 25 to 30%, one or more peripheral joints, particularly those of the lower limbs, exhibit evidence of an arthritis which is clinically and pathologically similar to rheumatoid arthritis.

The manubrio-sternal articulation is frequently involved, and less commonly the xiphi-sternum, acromio-clavicular, sterno-clavicular, costo-sternal and temporo-mandibular joints are the sites of painful, tender, inflammatory lesions.

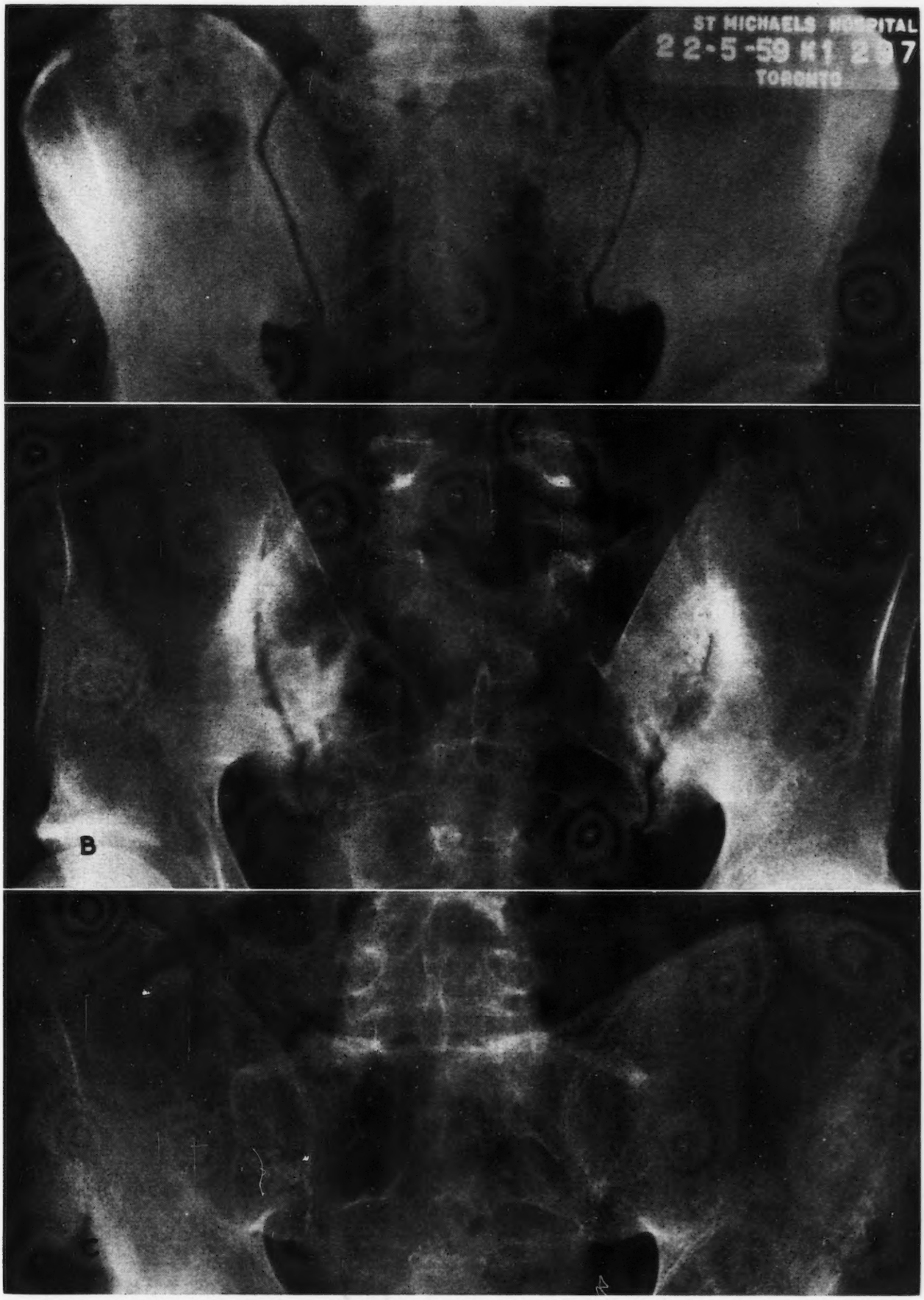

Fig. 3—(A) Radiographic appearance of normal sacro-iliac joints with uniformly regular articular space, well-defined clear-cut margins, and even density of adjacent bone. (B) Early sacro-iliac changes in ankylosing spondylitis. Joint outlines are hazy and blurred, the articular space appears unevenly widened, and its margins reveal erosions with patchy sclerosis of adjacent subchondral bone. (C) Late sacro-iliac changes are seen. The joint spaces have been obliterated by bony fusion. As ankylosis has progressed, the subchondral sclerosis has faded and the bone structure of the sacrum and ilium is of less than normal density.

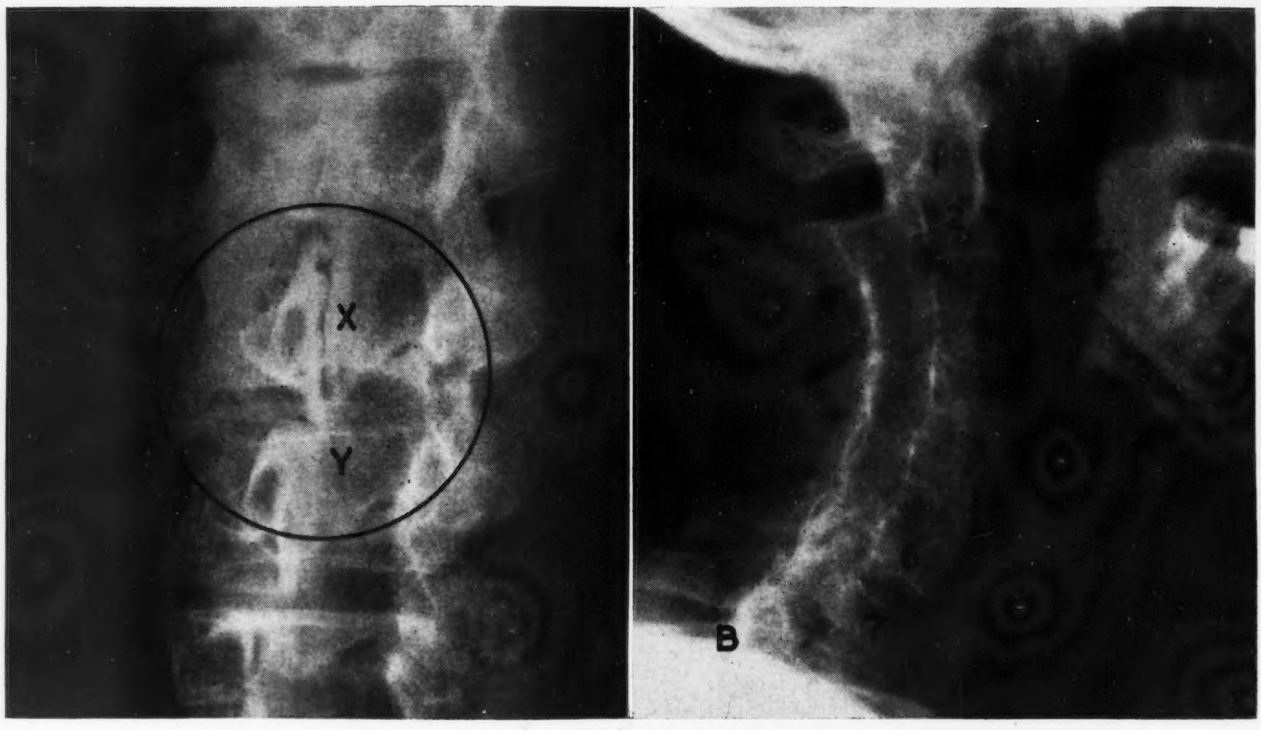

Fig. 4.—(A) Oblique radiograph of lumbar spine demonstrating the intervertebral apophyseal facets of a patient with ankylosing spondylitis. Apophyseal joint —X— reveals irregularity of articular space, erosions of its margins, and sclerosis of adjacent subchondral bone. Apophyseal joint —Y— has been obliterated by uniform bony ankylosis. (B) Lateral radiograph of cervical spine showing bony fusion of the apophyseal facets from C1 to C6 level. The facet at C6-C7 reveals a remnant of its joint space with well-marked sclerosis of the marginal bone.

About 10% of patients exhibit tenderness of the heels, over the plantar or posterior aspects of the calcanei, with or without calcaneal spur formation.

LABORATORY FINDINGS

The sedimentation rate may show little or no elevation in as many as 20% of patients, but is usually moderately increased and in severe cases may be grossly elevated.

Slight to moderate "secondary" anæmia and leukocytosis are not uncommon.

The serological reactions for rheumatoid factor, using the sensitized sheep cell agglutination, F-II latex fixation and bentonite flocculation tests, are characteristically negative.[1]

RADIOGRAPHIC CHARACTERISTICS

The earliest x-ray abnormalities nearly always involve the sacro-iliac joints in the form of blurring and haziness of their outlines, pseudo-widening of the joint space, irregular punched-out erosions of their margins and sclerosis of the adjacent subchondral bone. These changes may progress to bony ankylosis and finally to complete obliteration of the joint spaces (Fig. 3).

Similar radiological changes involve the intervertebral apophyseal joints, with an irregular distribution; the process tends to progress proxi-

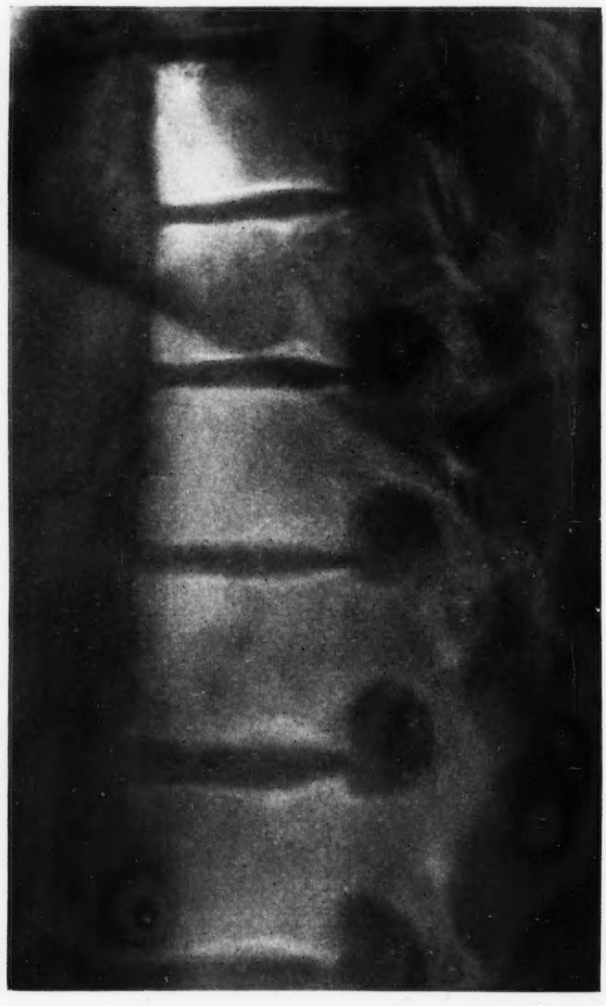

Fig. 5.—Lateral radiograph of the thoracic spine illustrating the "squaring-off" phenomenon. The corners of the upper three vertebral bodies are practically right-angled and their anterior borders are straightened out. In contrast, the lower vertebral body has a normally concave anterior border and its anterior corners have normal angles of less than 90°.

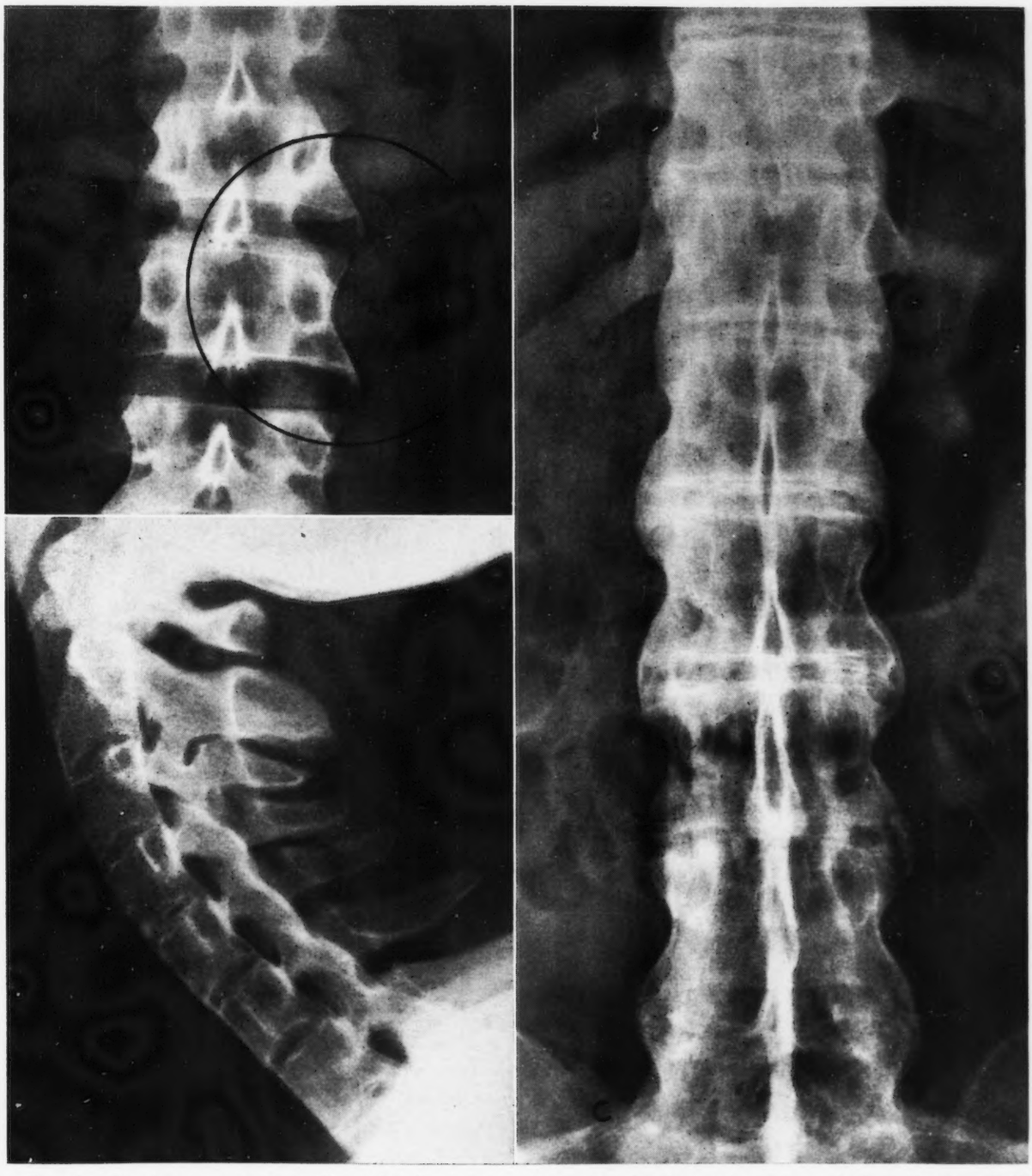

Fig. 6.—(A) Antero-posterior radiograph of upper lumbar spine showing early paravertebral ossification. Delicate linear spicules of new bone project from the infero-lateral angles of the bodies of the 2nd and 3rd lumbar vertebræ along the outer margins of the intervertebral discs and inner aspect of the paravertebral ligaments. (B) Lateral radiograph of cervical spine showing continuous intervertebral bony bridging due to ossification along both anterior and posterior spinal ligaments. (C) Antero-posterior radiograph of lower thoracic and lumbar spine showing extensive intervertebral bony bridging due to ossification along the paravertebral ligaments and disc margins. Ossification is also evident along the interspinous ligament in the mid-line of the lumbar (so-called "bamboo-spine").

mally for a variable extent through the lumbar spine, and in more advanced cases extends through the thoracic and later the cervical regions (Fig. 4).

Comparatively early in the disease, the thoracic and lumbar vertebral bodies frequently show a straightening out of their normally slightly concave surfaces, giving them a "squared-off" appearance (Fig. 5).

Calcification or ossification occurs at first in the annulus fibrosus of the intervertebral discs and later along the paravertebral and ilio-lumbar ligaments. Such paravertebral ossification usually begins in the lower thoracic and upper lumbar regions and gradually extends to involve other levels. In severe cases it may progress to complete intervertebral bony bridging throughout the entire spinal column, producing a rigid "bamboo-spine" (Fig. 6). At times, similar calcification or ossification may involve other ligaments including those of the extremities as well as the spine (Fig. 7).

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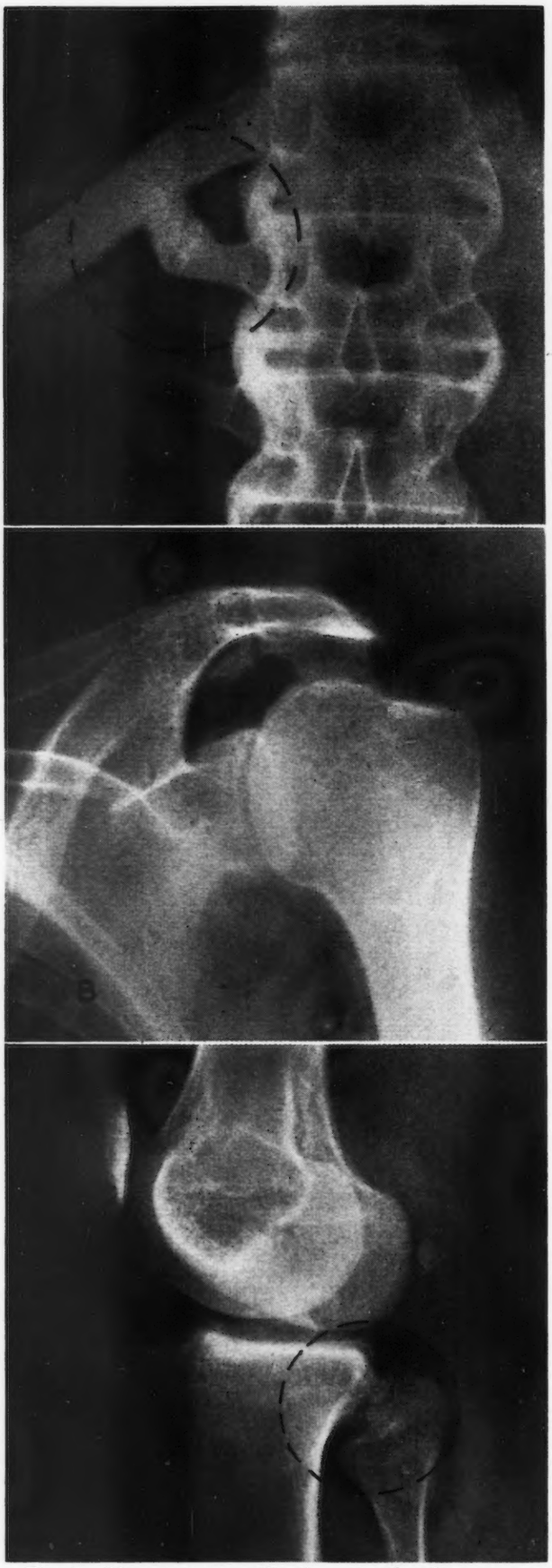

Fig. 7.—Ligamentous ossification at other less common sites in patients with ankylosing spondylitis. A.—Ossified lumbo-costal ligament between L1 transverse process and neck of 12th rib. B.—Uniform ossification of coraco-clavicular ligament at the shoulder. C.—Ossification of the fibular capitular ligaments traversing the anterior and posterior aspects of the proximal tibio-fibular articulation at the knee.

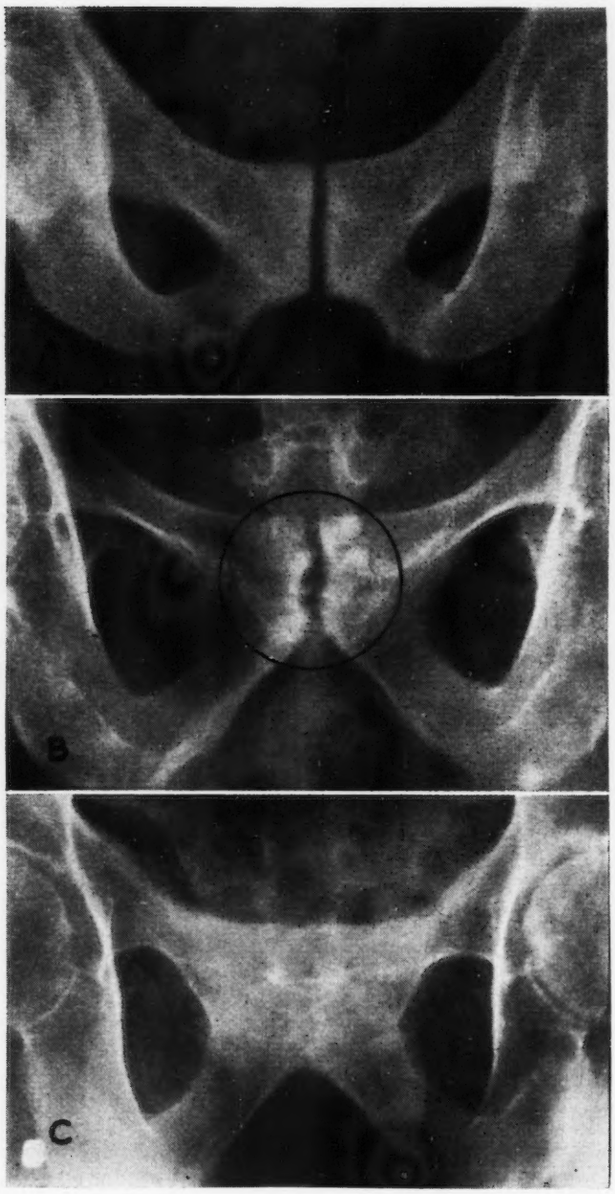

Fig. 8.—A. Normal symphysis pubis with regular interpubic space, clear-cut margins and uniform density of adjacent bone. B.—Early changes in pubic symphysis in ankylosing spondylitis. The margins are hazy in outline with irregular erosions and patchy sclerosis of adjacent bone. C.—Late changes in pubic symphysis in ankylosing spondylitis. The synchondrosis has been obliterated by uniform bony fusion. The evolution of these changes in the pubic symphysis is strikingly similar to that observed in the sacro-iliac and apophyseal joints and in the manubrio-sternal synchondrosis.

Synchondroses such as the symphysis pubis, manubrio-sternum, and xiphi-sternum may reveal irregular erosions of their margins which occasionally progress to bony fusion (Figs. 8 and 9).

Irregular surface erosions and new bone formation frequently occur at sites of fascial, ligamentous or muscular attachments, notably over the ischial tuberosities, the lateral surfaces of the iliac bones, the inferior aspects of the calcanei in the form of calcaneal spurs, the femoral trochanters, and occasionally at other locations in the extremities (Figs. 10 and 11).

The extent of these radiological changes varies greatly from patient to patient. Not uncommonly,

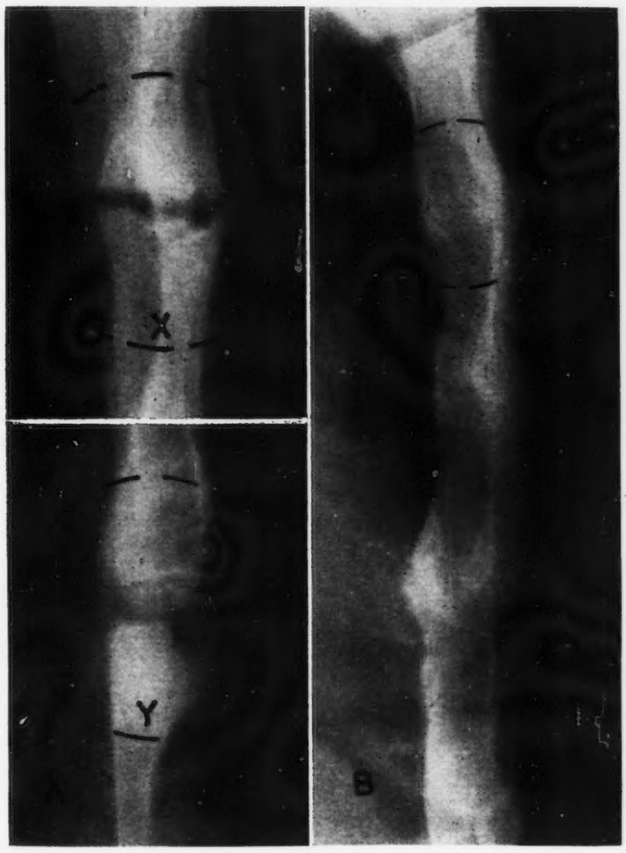

Fig. 9.—(A) Lateral radiograph of sternum illustrating irregular erosions of the margins of the manubrio-sternal synchondrosis —X—; and the xiphi-sternal articulation —Y. (B) Lateral radiograph of sternum illustrating late stage of manubrio-sternal involvement with uniform bony fusion of this synchondrosis.

x-ray abnormalities remain confined to the sacro-iliac joints, no other spinal or extra-spinal changes being demonstrable. In other instances the various x-ray findings described above occur in a great variety of combinations and degrees. X-ray changes in peripheral joints, when present, may resemble those of rheumatoid arthritis.

COMPLICATIONS

Recurring attacks of iritis or uveitis are the most common complication of ankylosing spondylitis, increasing in prevalence with increasing duration of the disease. These attacks of ocular inflammation usually subside completely with no residua but occasionally, after repeated recurrences, synechiæ, visual impairment or blindness may ensue.

A small number of patients exhibit an unusual cardiovascular lesion involving mainly the aortic valve and proximal aorta, which appears to be specific for this disease. Its major clinical manifestations are aortic regurgitation and prolonged atrio-ventricular conduction, and less commonly pericarditis. This "spondylitic heart disease" usually runs a prolonged course, but in time may eventuate in cardiac failure which may be the cause of death.[2]

Secondary amyloidosis, affecting the kidneys predominantly, is a rare complication which may result in a nephrotic syndrome, gradual failure of renal function and death.

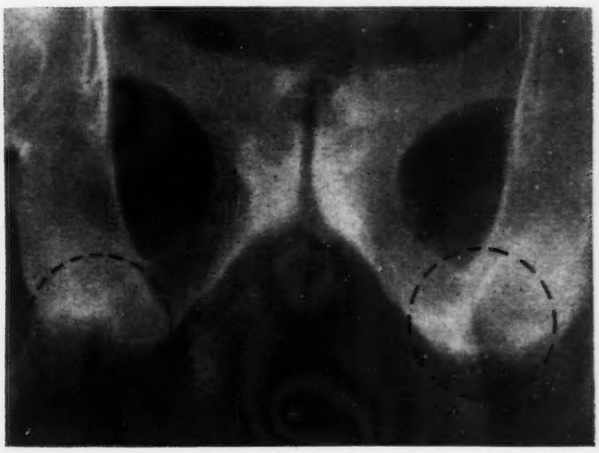

Fig. 10—Irregular osteolytic erosions of the ischial tuberosities. Such lytic lesions usually precede the production of irregular new bone illustrated in Fig. 11.

TREATMENT

The following general measures constitute the fundamental principles of care of the spondylitic patient: (1) The provision of adequate rest. This does not necessarily entail cessation of work except for the small proportion of patients who are badly disabled by severe, active disease. In some cases, a physically strenuous occupation may require modification or a change to lighter employment within the patient's limitations, but commensurate with his abilities, skills and training. (2) The use of a firm, non-sagging sleeping surface with boards under the mattress. (3) Daily physical therapy procedures involving the application of suitable forms of local heat followed by a specific program of therapeutic exercises, including deep breathing exercises and constant observance of proper postural habits. Most patients require encouragement, explanation and repeated instruction regarding these techniques and their importance in maintaining functional ability and preventing or minimizing deformity. (4) Maintenance of optimum nutrition with a full, well-balanced diet. (5) When required for relief of pain and stiffness, the regular administration of salicylates in adequate doses which may amount to as much as four, or occasionally five, grams daily.

This program, modified to meet the needs of each patient, should be observed faithfully whether or not other so-called "specific" forms of treatment are employed. Many patients do quite well on this regimen alone.

If pain and spasm persist and result in significant disability, phenylbutazone has proved particularly useful in doses of 100 mg., three to four times daily, and sometimes in smaller doses. While beneficial to many patients, its effects may, however, be disappointing to some and precautions must be observed to avoid its well-known toxic effects.

Deep x-ray therapy also may be followed by relief of pain and spasm during active phases of

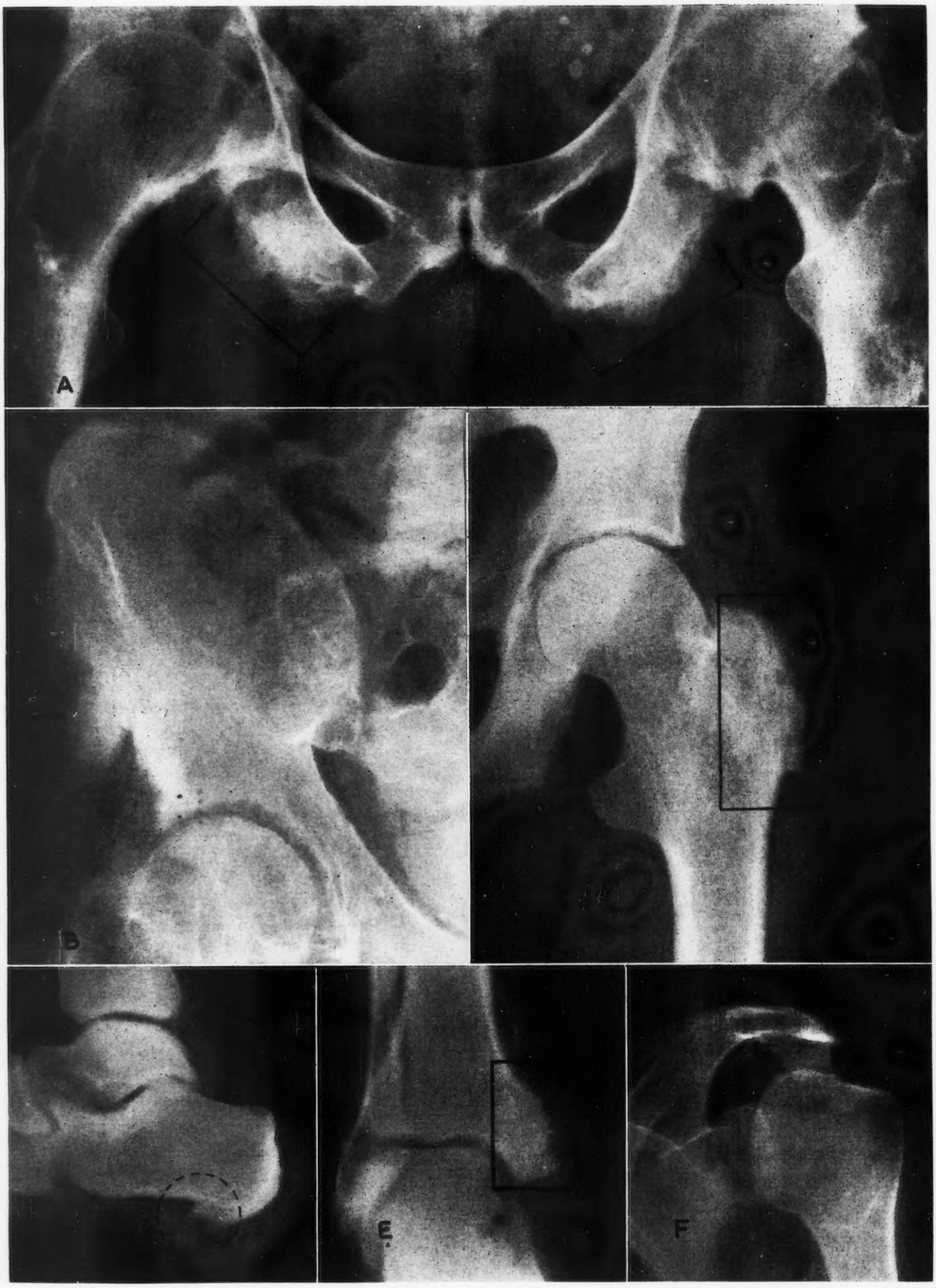

Fig. 11.—Irregular new bone formation at sites of muscular ligamentous and fascial attachments to bony surfaces.—(A) Over the ischial tuberosities.—(B) Over the lateral aspect of the ilium.—(C) Over the greater trochanter of femur.—(D) Over the plantar surface of the calcaneus in the form of a calcaneal spur.—(E) Over the medial malleolus of the tibia.—(F) Bar of new bone extending from the interior surface of the acromion.

the disease in some, but not all, cases. There is no convincing evidence that it halts progression of the disease or results in permanent remission. The development of leukæmia several years after roentgen therapy is now well documented and while it occurs in only a small proportion of patients, this potential hazard must be recognized and weighed against the probability of concrete benefit to the majority of patients so treated.[3]

Cortisone or other corticosteroid analogues may assist in the rehabilitation of some who have not responded satisfactorily to other measures, but these hormones are not required or indicated for the majority of patients and their prolonged administration may result in undesirable and occasionally serious effects.

Mr. Arthur Smialowski and the Department of Photography, St. Michael's Hospital, Toronto, provided valuable assistance in the preparation of illustrations.

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RÉSUMÉ

La spondylose rhizomélique ou spondylarthrite ankylosante est un trouble inflammatoire d'origine inconnue affectant les articulations sacro-iliaques et apophysaires de la colonne vertébrale, les surfaces osseuses au point d'attache des ligaments, muscles et aponévroses et les synchondroses. En dépit de ressemblance entre elles, la spondylarthrite et la polyarthrite chronique évolutive semblent deux entités distinctes. Dans les deux tiers des cas le début est lent et insidieux. La majorité des symptômes se rapportent à la région dorso-lombaire sous forme de douleurs sourdes avec extension ascendante le long de la colonne à mesure que l'affection progresse. Le malade accuse de la rigidité augmentée par le froid, l'humidité, et la grande activité physique et soulagée par la chaleur, les salycilates et des exercices modérés. Le malade se plaint de fatigue et d'une sensation de constriction de la poitrine et de l'abdomen. L'examen clinique révèle une diminution dans la flexibilité de la colonne surtout dans la région lombaire. La posture est affectée par le redressement de la courbure lombaire et le malade prend une apparence simiesque. Des spasmes musculaires sont observés. Les épreuves de laboratoire peuvent montrer une vitesse de sédimentation élevée ainsi qu'une certaine anémie et une leucocytose. A la radiographie l'articulation sacro-iliaque perd de sa netteté et l'os adjacent montre de la sclérose. Les corps vertébraux thoraciques et lombaires revêtent une apparence de bloc comme le montre la Fig. 5. On découvre aussi une ossification para-vertébrale avec syndesmosphytes qui débute habituellement dans la région dorso-lombaire et qui s'étend par la suite dans les deux directions. La colonne évoque alors l'aspect d'une tige de bambou. Parmi les complications notons l'iritis et l'uvéite qui peuvent quelquefois créer des synéchies et même causer la cécité. On peut aussi trouver des atteintes à la valvule aortique et même une péricardite. L'amylose secondaire ne se manifeste que rarement. Le malade atteint de spondylose doit pouvoir se reposer sans nécessairement interrompre toute activité physique. Il couchera sur une surface ferme et recevra des applications de chaleur locale suivies d'un programme d'exercices thérapeutiques comprenant des exercices respiratoires. La nutrition doit être maintenue à son niveau optimum grâce à un régime bien équilibré. La douleur et la rigidité peuvent répondre à l'administration de salycilate. Dans les cas rebelles l'administration de phénylbutazone a déjà donné des résultats intéressants. Lorsque l'affection est en phase d'activité la radiothérapie peut soulager la douleur et le spasme sans nécessairement interrompre l'évolution de la maladie. On peut aussi avoir recours à la cortisone et aux autres stéroïdes.

CASE REPORT

FUNGOUS GRANULOMA OF THE LOWER LEG DUE TO TRICHOPHYTON MENTAGROPHYTES

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Ottawa, Ont.

NUMEROUS REPORTS have appeared in the North American literature on mycotic granulomas of the leg due to *Trichophyton rubrum*.[1-3] Some European articles[4-6] indicate that rarely *Trichophyton mentagrophytes* may be the cause.

Mrs. H.S., aged 36, was referred to me by her family doctor* for diagnosis and treatment of a non-healing "sore" on her right anterior lower leg. The "sore" appeared in November 1958. There was no known exposure to animals with ringworm.

*Dr. Donald Robertson of Morrisburg, Ontario.

Fig. 1.—Scaly dermatitis on anterior lower leg (from 35 mm. colour transparency).

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Fig. 2.—*Trichophyton mentagrophytes* growing on Sabouraud's medium.

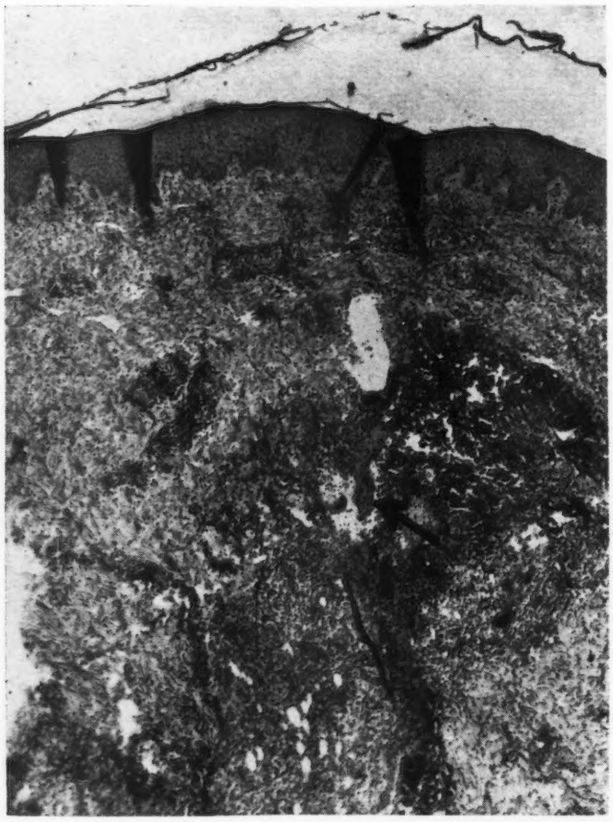

Fig. 3.—Section showing portion of degenerating hair follicle (arrow) surrounded by extensive inflammatory granulomatous infiltrate (Hæmatoxylin and eosin, × 40 approximately).

In February 1959, she developed a group of inflammatory crusted follicular granulomas interspersed with and surrounded by a superficial scaly dermatitis (Fig. 1). A few of the follicular lesions had left smooth atrophic scars. The lesion measured 5 cm. in diameter. There was no clinical evidence of other cutaneous fungous disease. KOH examination of epidermal scrapings revealed branching mycelia. Culture on Sabouraud's medium producing a growth of *Trichophyton mentagrophytes* (Fig. 2). Histological examination (Fig. 3) showed a granulomatous infiltrate involving most of the dermis and some of the subcutaneous fatty layer. The granuloma was made up of accumulations of polymorphonuclears (some were forming microabscesses) surrounded by inflammatory granulation tissue. In one area the remains of a hair follicle were present. Examination for fungi by special stains was negative.

The lack of involvement of the toes or feet by the fungus is most unusual.

SUMMARY

A case of fungous granuloma of the lower leg due to *Trichophyton mentagrophytes* has been presented.

Mr. M. Smith of the Ottawa Civic Hospital took the photomicrograph.

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SHORT COMMUNICATIONS

THE QUALITY CONTROL LABORATORY OF THE ETHICAL PHARMACEUTICAL MANUFACTURER*

EVERY ETHICAL pharmaceutical manufacturer worthy of the name maintains a quality control laboratory to ensure that every product of his manufacture conforms to his label claim before it is released for sale. A corollary of this is that only those drugs produced by ethical manufacturers who maintain such quality control laboratories can be considered completely dependable.

The quality control laboratories of the pharmaceutical industry maintain a close liaison with the Food and Drug Directorate of the Department of National Health and Welfare. The Directorate

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is responsible, under the Minister, for the enforcement of the Food and Drugs Act, and for the development of Regulations under the Act. The industry's control laboratories maintain their contact with the Directorate both through individual company effort and through the technical section of the Canadian Pharmaceutical Manufacturers Association.

Many of the functions of the quality control laboratory can be visualized by considering the part played by it in the development of a new drug. When the synthesis or extraction of a new drug is complete, and its study in animals reveals that it has useful pharmacological properties and a sufficiently low toxicity, it is ready for human trial.

At that point the quality control laboratory, in collaboration with those who have developed the drug, must establish specifications to define its identity, purity and potency. These specifications must in turn be supported by analytical methods by which conformity to specification can be determined. Usually one or more new methods must be developed for this purpose. In many instances, methods suitable to the drug in its pure state must be modified or replaced by others in working with its dosage forms.

The new drug is now ready for distribution to investigators. If it survives its clinical trials (and a high proportion do not), it is almost ready for the market. Before it can be marketed, a "New Drug Submission" must be made to the Department of National Health and Welfare. At this time, the control laboratory re-examines the specifications and methods which were developed for the clinical trial lots. Experience may have shown that they need modification or extension. It is also necessary to be sure that they will prove adequate for the larger scale of operation that will be necessary in producing commercial quantities. These methods form a part of the "New Drug Submission", along with the reports of the clinical trials, the animal toxicity, the manufacturing procedures and the labelling.

Even before material is distributed for clinical trial, studies of the stability of the drug and its dosage forms are begun by the control laboratory. This work is continued concurrently with the clinical trial, and on the basis of the results obtained the development group can introduce modifications in the formula to overcome instability, if it should exist. Perhaps the results will suggest the inclusion of an anti-oxidant, the exclusion of air in processing, a tighter limit on moisture, a different solvent or a different method of packaging. The stability studies do not stop with the introduction of the product to the market but are continued, for years if necessary, to be sure that the drug and its dosage forms are stable, and will retain labelled potency and quality during reasonable shelf life.

The present-day quality control laboratory is equipped to carry out a wide range of biological, microbiological, chemical and physical testing procedures. These include potency, pyrogen and toxicity tests in the biological field; sterility of injectables, and potency of antibiotics and vitamins, using microbiological techniques; and a wide range of potency, identity, and purity assays in the fields of chemistry and physics.

In the past few years, many ingenious and elaborate instruments have been developed to give sensitivity to the analyst's hand and keenness to his vision. Spectrophotometers have been developed for light measurement in the visible, the ultraviolet and the infra-red regions of the spectrum. All of these are indispensable in today's control work. Extremely sensitive balances are available to weigh the microgram quantities encountered in the dosage forms of some of our very potent drugs. Electronic devices are now in use to measure and record the temperatures of the rabbits used in the pyrogen test on injectables. There are many others.

Many new techniques of analysis have been introduced also. Radioactive isotopes help in the assay of a number of drugs; radioactive cobalt, for example, can be used to determine vitamin B_{12}. Column chromatography, paper chromatography, and more recently, gas chromatography are very sensitive tools in the isolation and assay of many drugs, both new and old. The use of infra-red spectrophotometry in assay work is steadily expanding.

The work of the quality control laboratory, on both new drugs and old, is time-consuming and costly. Much of it may seem at times redundant. It is extremely rare that an injection is found to be non-sterile or pyrogenic or that an active ingredient has been omitted, or added in excessive quantity. Nevertheless, no ethical manufacturer is willing to run the minute risk that such a thing may happen. Hence, even though the cost of the control work may represent 10 to 15% of the production cost, every lot is checked for potency, sterility, safety and all the other attributes that are appropriate.

Most of the work of the quality control laboratory goes unobserved by the physician or his patient. Like the air we breathe, quality control is apparent only when it is lacking.

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SARAN PLASTIC BAGS AS CONTAINERS FOR BREATH SAMPLES

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and D. M. LUCAS, M.Sc.,† *Toronto*

SEVERAL INSTRUMENTS, such as the Breathalyzer, have been designed to analyse expired air accurately for the presence of alcohol. Their practical use at present is chiefly confined to the estimation of alcohol in breath samples taken from motor vehicle drivers involved in traffic accidents.

While at first it was visualized that such instruments might be employed for on-the-spot analyses of breath of motor vehicle drivers suspected of drinking before involvement in a traffic accident, time has proved that their use in a traffic squad car is very limited. These instruments must be installed in a laboratory or a police headquarters where a trained operator can use them under controlled conditions.

Two difficulties may be encountered in conducting breath analysis. When the Breathalyzer is used, the subject must breathe through a tube into a small metal chamber of exact dimensions, where the last portion of expired air is entrapped automatically and is analysed later. For all practical purposes this entrapped air may be considered alveolar air. If a driver were seriously injured, he might not be able to be moved to a police station to have a breath analysis carried out. Secondly, in some cases a period of time elapses before a traffic officer is able to transport a motor vehicle driver to a police station for a breath test by an analyser. It is obvious that a simple breath-sampling apparatus would enable an officer to obtain a breath sample shortly after an accident and obviate these two difficulties.

A number of different materials have been employed in the form of bags to contain breath samples for analysis. Harger, Lamb and Hulpieu,[1] in 1938, used rubber balloons to collect breath samples which were to be analysed in the Drunkometer immediately. In 1949, Harger, Turrell and Miller[2] devised a flexible aluminum bag for breath sampling. Lucas *et al.*,[3] in their traffic survey of Toronto in 1951, wished to collect and store for short periods samples of breath taken from both accident and non-accident motor vehicle drivers at the scene of a traffic accident. They prepared bags from polyethylene in which breath samples could be stored for an hour or so without serious loss of alcohol.

Such researches focused attention on the usefulness of a suitable container for breath samples. Kalow, Lucas and McColl[4] had shown that the "alcohol half-time" of rubber balloons was about 15 minutes (the time required for loss of half the alcohol in the container) and of polyethylene bags about three hours. Some longer periods of storage might be necessary, and careful investigation was begun to find a plastic which, when formed into a suitable bag, would store breath samples containing alcohol, with very little or no loss for 24 hours. Aluminum foil, polyethylene, nylon film and canvas film were found unsuitable. Further experiments with pliofilm, cryovac and polyethylene proved that alcohol escaped too easily through them. Finally, it was found that Saran 100-gauge was a suitable plastic. It is a polymer of vinylidine chloride and vinyl chloride. It is a transparent, flexible material impermeable to water and most gases and is unaffected by many chemicals. The use of double-wound Saran in making the containers reduced the possibility of having minute holes develop in each layer in the same site. The real problem which confronted us was that Saran must be sealed electronically; for different designs of containers, expensive electronic sealers had to be fabricated. Space does not permit a detailed account of the types of bags designed, the difficulties encountered in the sealing, or all the tests applied to ensure the suitability of Saran. We are indebted to the following companies in Toronto: Dow Chemical Company, Mastex Industries Limited and Central Scientific Company, for their co-operation in the manufacture of the bags.

The adsorption of alcohol on Saran was estimated by pair-filling two bags with gas from an "artificial drunk" (an apparatus designed to equilibrate air and a solution of alcohol of known concentration); one bag was half-filled. Since no significant changes in alcohol concentration were observed with various amounts of alcohol, adsorption of alcohol on Saran was evidently negligible.

The effect of storage was measured in the Department of Pharmacology with a number of bags by filling them with gas from an "artificial drunk" and analysing the gas in them after five minutes' standing, and after 24 hours' storage. In 12 analyses the loss after 24 hours was $3 \pm 3\%$. When bags, filled with gas, were heated by wrapping them in an electric heating pad at 60° F. for five minutes, no appreciable change in alcohol content occurred. A further test on the effect of wetting the outer surface was carried out by filling bags with gas from an "artificial drunk", rolling them in water for some minutes and storing them in the wet state for eight hours. Again, no significant loss of alcohol was noted.

The final design of the collecting bag is shown in Fig. 1. It is somewhat tubular in form and is drawn out at each extremity to small tubes; one serves to hold a mouth-piece and the other is so constricted that the bag becomes inflated when the breath is blown through it; the capacity is about 500 c.c. When this bag is used, both small tubes are folded over and clamped just at the end of expiration. Each bag must be tested for leaks before it is used, by filling it with air, clamping it and immersing it

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†Laboratory of the Attorney General of the Province of Ontario.

Fig. 1

in water. After this test, it must be filled with pure air and tested in the Breathalyzer for contaminants.

Sampling bags of this type were repeatedly tested in the Department of Pharmacology on subjects who had consumed alcohol. Their breath was tested for alcohol after it was blown directly into a Breathalyzer, and after it was blown into a bag and the content of the bag was analysed in the Breathalyzer. As the results of these analyses showed no appreciable differences, bags were sent to the Laboratory of the Attorney General of Ontario where numerous tests were carried out by Mr. D. M. Lucas, a member of the staff of the laboratory.

D. M. Lucas confirmed the findings reported above on the changes due to storage and added several important contributions. Samples of breath taken from 19 subjects arrested for drinking and driving offences were analysed in the Breathalyzer. A second sample from each was taken in a sampling bag and analysed in the Breathalyzer after storage for periods of nine to 62 hours. The greatest loss observed was 0.03%, after 62 hours, on one sample which had an initial alcohol concentration of 0.21%. The greatest gain was 0.01% on two samples which had an initial alcohol concentration of 0.19% in periods of storage of 38 and 62 hours. These changes represent a loss or gain caused by methods of sampling and storage, and for practical purposes may be considered negligible.

When bags containing alcohol and water vapour were subjected to freezing, the increased condensate did not have any significant effects on the analytical results. It was noted, however, that the Saran became more brittle and subject to tear.

In the practical tests it was found that a police officer could be trained quickly to use the bags properly and that he experienced no difficulty in so doing. In fact, in several cases it was simpler to obtain a sample in a bag than in the Breathalyzer because of the subject's physical condition.

CONCLUSION

The Saran bags have been found to be quite practical for use in case work. For this work they are cleaned and tested before they are stored in sealed containers, and after samples of breath are taken the bags are replaced in sealed containers until they are tested within 48 hours of the collection time. They are presently in use in 16 areas of the province of Ontario where great distances make the transport of a subject to the Breathalyzer impractical. They are also valuable where it is important for a physician to know whether a patient's condition is due to alcohol or not. In these cases a sample of breath can be collected from the patient and quickly tested by a trained police officer, and the results soon made known to the physician. Such tests, by ruling out alcohol intoxication, have assisted in making a proper diagnosis and, therefore, in ensuring the right treatment of several persons who might otherwise have been treated as intoxicated. Saran bags should serve a useful purpose in the proper handling of arrested persons and the administration of justice.

This work was aided in part by a grant from the Alcoholism Research Foundation.

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IT'S LATER THAN YOU THINK

Thousands of busy doctors have recorded their views on the vital topic of Health Insurance by completing and returning the C.M.A. questionnaire. We suspect that in many instances the papers have been put aside for later consideration. If this is your situation, we urge that you attend to the matter now because the analysis of replies will be undertaken in early April and your opinions should be included.

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RESPONSIBILITIES OF HOSPITAL TRUSTEES

There is still far too much unnecessary confusion about the relative roles and responsibilities of the medical staff, the administrative staff and the board of trustees of hospitals.

In an address to the Institute for Trustees, Administrators and Accountants held by the Maritime Hospital Association at Moncton last November, Dr. W. I. Taylor of Toronto outlined the areas of responsibility of hospital trustees for the activities in any institution, and cleared away some of the areas of confusion. He began by stating that trustees of any hospital had a moral as well as a legal responsibility, and that these legal and moral obligations, like the legal and moral obligations in marriage, bound a hospital trustee to his hospital. This situation sometimes led to an apparent conflict between what was legally required and what seemed morally right, between what was economically possible and ideally desirable, and this created one of the heaviest responsibilities of the hospital trustees.

As to the specific areas in which trustees were responsible, Dr. Taylor said that these were laid down quite clearly in the Standards for Accreditation of Canadian Hospitals. The Basic Principles laid down in the Standards say that "the trustees are legally and morally responsible to the patient, the community and the sponsoring organization to insure the safety of the patient and promote his welfare and they should do this by provision of an adequate physical plant, good administration, facilities for certain essential services and proper medical and nursing staffs." The first responsibility of a trustee is the operation of the hospital as a hospital. It is necessary to clear our minds of the idea that the advent of a government-sponsored hospital insurance scheme has made government responsible for running community hospitals. This is entirely false; the government is the paymaster, not the administrator or organizer. Nevertheless, if government pays money to a hospital it has a right to require justification of its expenditures, and if the board of trustees of any hospital fail to fulfil their legal and moral responsibilities, government in defence of the public interest must do so. Dr. Taylor added significantly that "the future of our voluntary hospital system may well be in the hands of hospital trustees".

Furthermore, he pointed out that the governing body is responsible to the community and the sponsoring organization for the *kind* of hospital provided. There is far too much enthusiasm for the building and equipping of more and more general hospitals, and far too little for the provision of chronic and convalescent care. There is also a tendency for communities and sections of communities to enter into competition in the provision of hospital facilities, sometimes in situations where a little more consultation and co-operation would prevent useless duplication of services. Moreover, there is a tendency for communities not to widen their horizons sufficiently in considering hospital care. In other words, they may feel the need for providing highly advanced equipment in a community, when at a reasonable distance away there is a bigger and better hospital centre with better trained physicians and surgeons to do the job. As Dr. Taylor reiterates, "It cannot be repeated too often that a hospital is people." The provision of complicated technical equipment is gratifying to local pride, but entirely useless unless the trained men to operate the equipment are available.

It is also the responsibility of a board of trustees to appoint a competent administrator and require competent administration. Too often, this extremely demanding and extremely technical job is entrusted to untrained people, because trustees and even some medical staffs have not yet appreciated the value of the trained administrator.

There is also a misconception as to the responsibility for determining standards of care within a hospital. It is often thought that this is the sole responsibility of the medical staff and that no one else should intervene. It is true that only the physician can judge the quality of medical care, but the trustees nevertheless have the responsibility to see that a certain standard of care is being provided. In this, they need only be guided by the standards of the Canadian Council on Hospital Accreditation.

Lastly, we are reminded that the board of trustees is responsible for appointing the medical staff and for ensuring that each physician is qualified and competent to do the things he is permitted to do in the hospital. Here again, many persons are under the misapprehension that this responsibility is that of the medical staff. It is certainly a heavy responsibility of the staff by delegation, but it is primarily and ultimately a responsibility of the board. The medical staff make recommendations to the board, but the board themselves must make the appointments because

they are legally responsible for them. Dr. Taylor remarks, "Let us hear no more nonsense then to the effect that every licensed practitioner has a right to hospital staff appointment, that privileges should be the same for all physicians, or that every physician is entitled to use the hospital as he sees fit to treat his private patients."

To sum up, the pattern for authority and responsibility for the work of the medical staff in a hospital is clearly defined in the Standards laid down by the Canadian Council on Hospital Accreditation. So long as these are consulted and applied, there need be no confusion in these important areas of control.

Editorial Comments

THE NEED FOR MORE CASE REPORTS

The reporting of cases in medicine is one of the most essential elements in the building up of medical literature. These reports act as indispensable bricks. Too often, however, they are not put into general service. The individual doctor in whose practice the cases occur uses them, and rightly so, in guiding him and enriching his experience; both in hospitals and in private practice there must be an inexhaustible mine of these professional nuggets (to vary the metaphor slightly).

It is their extraction and refinement for general instruction through the medium of our Journal for which we appeal. It is customary to give the major amount of space to "papers" rather than to case reports, but this should not be taken as an index of the relative degree of importance or interest. A case report can be made the text of significant teaching, with the added impressiveness often associated with short rather than long "sermons".

It is these reports even in very short form which add balance, effectiveness and flavour to a journal such as ours.

PREVENTION OF THROMBOEMBOLISM

The usefulness of anticoagulant therapy in the prevention of thromboembolism in injured elderly patients has been proved by Sevitt and Gallagher (*Lancet*, 2: 981, 1959) in an admirable example of scientific method in medicine. In a carefully designed and controlled trial, the incidence of major embolism was 18% in controls and nil in patients receiving prophylactic phenindione.

The trial was restricted to patients over 55 years of age with either a subcapital or intertrochanteric fracture of the femur. Chance distribution of cases was ensured by giving phenindione to patients admitted on even days of the calendar month; those admitted on odd days formed the controls. The phenindione group comprised 150 patients, but in 15 of them the drug was contraindicated. The control series also comprised 150 cases. Four of these were excluded because they had been given phenindione for other reasons (e.g., suspected coronary thrombosis).

All surviving patients were followed up for at least three months from the time of injury; every patient was accounted for. There were 43 cases of clinically diagnosable thrombosis in the control series (28.7%), compared with only four cases in the phenindione series (2.7%)—a reduction of over 90% in frequency. In two of the four failures, thrombosis was probably already present before admission, and in the other two some difficulty was encountered in that the plasma prothrombin levels were ineffectively lowered over a five- and a six-day period respectively. This illustrates the facts that thrombosis may sometimes develop before admission or even before injury, and that the early institution of effective dosage is needed for full protection.

With regard to post-mortem evidence, reliance on the classical clinical criteria underestimates the incidence of fatal embolism. In their series only about half of the patients with fatal embolism collapsed and died within minutes or hours. The manner of death varies and can also be gradual deterioration, acute onset of congestive cardiac failure, or a sudden attack of hypotension possibly resulting in acute renal failure. An 86% post-mortem rate was achieved. During this period there were 42 deaths (27 were non-embolic) in the control series and 25 deaths (23 were non-embolic) in the phenindione series. The two deaths from embolism in the phenindione series occurred after therapy had stopped, so were not really due to failure of current prophylaxis. Therapy may usually be discontinued in patients who become mobile and active, but the problem arises of when to stop the drug in those elderly inactive patients who may never become properly mobile or who spend most of their time in bed.

Careful post-mortem examination of the deep veins revealed that thrombosis was very common and extensive in the control series, and absent or slight in the phenindione series, except for three special cases in which phenindione had been discontinued days or weeks before death. (The two cases of fatal embolism in the phenindione series were also the ones which had thrombi in veins and had had the phenindione discontinued.) Thus no patient developed significant deep vein thrombosis while under the influence of phenindione.

In regard to safety, the surgeons reported that the wounds of patients under phenindione bled no more than the controls during the hip operations. However, it must not be assumed that the freedom from undue hæmorrhage found in nailing and pinning operations on the hip applies to all surgery.

The prevention of thrombosis was reflected in the prevention of embolism. No case of embolism occurred in patients under the influence of phenindione, compared with a total of 27 cases (18%) of all degrees of pathological and clinical embolism among the controls.

It is reasonable to advocate prophylactic protection at least for those particularly at risk of embolism—that is, those over 50 years of age who are about to undergo a period of bed rest for longer than two or three days and in whom anticoagulant

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therapy is not otherwise contraindicated. Major contraindications to anticoagulant drugs are recent melæna, hæmatemesis or hæmoptysis, peptic ulceration, and hæmorrhagic diathesis.

VIRAL INFECTIONS OF THE CENTRAL NERVOUS SYSTEM

Accurate determination of the viral etiology of poliomyelitis and the aseptic meningitis syndrome has been greatly facilitated through the widespread use of tissue culture techniques.[1-3] Lennette *et al.*[4] have recently shown that 44% of 1407 California patients who developed probable viral disease of the central nervous system between July 1955 and December 1957 excreted an enterovirus in the fæces. Poliovirus, principally type I, was excreted by 24% of patients, 14% shed Coxsackie virus and 6% yielded unidentified ECHO viruses. Of 497 patients with paralytic poliomyelitis, 54% excreted poliovirus; but non-paralytic patients excreted Coxsackie or ECHO viruses frequently, and poliovirus infrequently. About 70% of unvaccinated paralytic patients yielded poliovirus, but of paralytic patients excreting virus who received two or more doses of poliomyelitis vaccine, few shed poliovirus and 25% yielded another enterovirus. Although it has been observed both in naturally infected individuals[5] and in those fed living attenuated poliomyelitis vaccines[6, 7] that no apparent inhibition of viral multiplication in the alimentary tract occurred following three doses of Salk-type poliomyelitis vaccine, the present results[4] suggest that prior vaccination may inhibit somewhat the multiplication of virus in gut tissues. The low rate of poliovirus excretion in vaccinated patients also kindles speculation whether another enterovirus alone may occasionally evoke paralysis, which has been reported for Coxsackie A7[8, 9] and for Coxsackie B5 and ECHO 2.[9]

Serological procedures alone suggested an etiological diagnosis in few patients who did not yield virus. About 10% of non-paralytic patients showed significantly rising mumps antibody levels; and 5% of patients with encephalitis showed rising antibody titres to an arthropod-borne viral antigen. However, 90% of paralytic patients who excreted poliovirus had elevated complement fixing antibody levels to poliovirus in convalescent sera, and 55% of these showed rising antibody titres. Although several groups of workers[10-12] have employed the complement fixation test extensively in enterovirus studies, the neutralization test using tubes,[2] reduction of plaque count,[13] metabolic inhibition,[14] or paper discs[15] is preferred by many investigators.

Since enteroviruses may sometimes be isolated from fæces of healthy persons[16, 17] it is essential to seek confirmatory evidence that the virus isolated from a patient's fæces actually caused infection,[18] either by isolation of virus from cerebrospinal fluid or by demonstration of a rising antibody titre. Serological results recorded by Lennette *et al.*[4] augment the etiological significance of viruses excreted in fæces.

Although Lennette *et al.*[4] include the terms "viral meningitis", "non-purulent meningitis" and "benign lymphocytic meningitis" in the diagnostic category "aseptic meningitis", the reason for placing non-paralytic poliomyelitis in a separate category is obscure. Their own results indicate that true "non-paralytic poliomyelitis", i.e. signs of non-bacterial meningeal irritation accompanied by fæcal excretion of poliovirus, occurs uncommonly in both categories "aseptic meningitis" and "non-paralytic poliomyelitis". We suggest that the term aseptic meningitis be used for all cases in which there are signs of fever, neck stiffness and pleocytosis of cerebrospinal fluid in the absence of bacterial infection.

In California during 1955, Coxsackie A9 and Coxsackie B2 viruses were isolated more frequently than other serotypes from non-paralytic patients. Coxsackie B5 virus became dominant during 1956, whilst in 1957 Coxsackie B4 was the most abundant serotype. Similarly an annual succession of dominant enteroviruses has been observed in Toronto and the northern United States.[19]

Although enteroviruses were isolated from 44% of patients with central nervous system disease, and a cause was suggested in additional instances on serological grounds, the etiological agent in almost 50% of non-paralytic cases remained undetermined. Further tests are evidently required to elucidate more clearly the etiology of viral disease of the central nervous system.

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Medical News in brief

EFFECTS OF UNBUFFERED AND BUFFERED ACETYLSALICYLIC ACID ON INTRAGASTRIC pH

Acetylsalicylic acid is very widely used in both buffered and unbuffered forms, the buffered forms having been evolved on the grounds that the drug affects gastric acidity in man and thus causes symptoms. In a recent series, Rubin and his colleagues of Boston (*New England J. Med.*, 261: 1208, 1959) compared the effects on gastric acidity of acetylsalicylic acid, a buffered salicylate preparation, and a placebo by measuring the gastric pH continuously with a glass electrode placed in the stomach. They performed 49 experiments on six men and one woman, all young and in good health. Subjects fasted before each experiment, and the results indicated that the magnitudes and time courses of the intragastric pH changes caused by both buffered and unbuffered acetylsalicylic acid preparations taken orally with water were not significantly different from the magnitudes and time courses of the pH changes produced by the same volume of water alone or with a placebo. The change in intragastric pH observed when two tablets of either buffered or unbuffered drug were administered with water depended almost entirely on the dilution of the acid gastric contents by the water itself, and not on the presence or absence of buffering materials in the drug preparation.

DISSEMINATED COCCIDIOIDOMYCOSIS

Coccidioidomycosis is an endemic disease in large parts of the Western and Southwestern United States. Almost every resident in these areas eventually acquires a primary infection, caused by inhalation of the chlamydospores of *Coccidioides immitis*. In most cases the resulting infection is so mild that it remains unnoticed; only a positive coccidiodin skin test at a later date will reveal that infection has occurred. Other individuals experience respiratory and general symptoms of varying degree as a result of chest lesions such as pneumonitis, cavitation, pleural effusion and spontaneous pneumothorax. Fortunately, in only a relatively few patients does coccidioidomycosis disseminate to extrapulmonary tissues and organs with the attendant severe morbidity and high mortality rates. In a recent paper (*Dis. Chest*, 36: 136, 1959) Stein discusses disseminated coccidioidomycosis, presents a few illustrative cases and outlines its present-day treatment.

Dissemination follows failure of the body to "focalize" the disease at its primary site. It is an endogenous reinfection and comes on shortly after the primary infection, of which it is a continuation. Coccidioidal pulmonary cavitation seems to confer immunity against dissemination. Dissemination involves every body tissue, excepting the intestinal tract. Multiple abscesses, spread widely throughout the body, are frequent, meningitis somewhat less so. The latter not infrequently shows temporary spontaneous remissions of varying duration.

The diagnosis rests mainly on bacteriological and serological studies rather than on clinical findings. Anergy renders the coccidioidin skin test unreliable in the disseminated form of the disease. The prognosis is grave because the mortality rate is at least 50 to 60%, especially in non-white individuals.

Many therapeutic agents have been tested unsuccessfully. A new antibiotic, amphotericin B or Fungizone, has benefited a small number of patients. It has, however, various undesirable side reactions which lead to interruption or discontinuation of its use in quite a few patients.

REMOVAL OF RADIO-OPAQUE FOREIGN BODIES

In the Kommunehospital, Aarhus, Denmark, Dr. Ratjen and his colleagues (*Danish M. Bull.*, 6: 273, 1959) have developed a stereoscopic method for the removal of radio-opaque foreign bodies, particularly those situated within the orbit and the eye. The method is particularly useful for foreign bodies which cannot be removed by a giant magnet or be located by the Berman electromagnetic locator. It depends on the production of images by two roentgen tubes simultaneously on the same fluorescent screen during the extraction. The viewer looks at the two images, and because the converging beams intersect at the site of the foreign body, he obtains a very accurate impression of the relative position of the body and the surgical instrument he is using. During fluoroscopic examination of the patient, it is easy to determine whether the foreign body is within the eye or outside it.

Use of an image intensifier renders the radiation dose delivered to the patient and the surgeon negligible. Preliminary experience with this technique, which is described in full by the authors, is highly satisfactory. It is reliable and can easily be performed by an ophthalmologist without special radiographic training.

LACK OF SYNERGISM IN AN ANTIBIOTIC COMBINATION

Attention has been drawn previously by Finland and his colleagues from Boston to the mistaken impression that certain combinations of antibiotics have a synergistic action on human patients. The most recent investigation of this problem by Hirsch and Finland is published in the *New England Journal of Medicine* (262: 209, 1960). They determined the effects of administering novobiocin in combinations with tetracycline on the antibacterial activity of the serum of eight normal young men, as measured in a twofold-dilution test in broth using four test strains of staphylococcus and streptococcus that were sensitive to one or both of these antibiotics. They failed to observe any synergistic effect of this combination in a 1:2 or 2:1 ratio in controlled tests of the sensitivity of the strains *in vitro*, and felt that the combined effect could be considered as additive or indifferent. This was also true of serum activity after ingestion of these antibiotics by the same subjects in the ratios mentioned above. One disquieting finding was that administering 500 mg. of tetracycline with 250 mg. of novobiocin resulted in a lower antibacterial activity in serum against a tetracycline-resistant staphylococcus as compared with the dose of novobiocin alone.

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NEW DRUGS

This listing of new products is based on information received from Dean F. N. Hughes, Faculty of Pharmacy, University of Toronto, and the *Canadian Pharmaceutical Journal*, to whom we owe thanks.

HORMONES

Hydrocortisone — ocular therapy: CORPHOS (Pr), Crookes-Barnes

Description.—A true solution of hydrocortisone-21-phosphate.

Indications.—To control ophthalmic inflammation.

Administration.—1 or 2 drops in the eye every 2 hours during the day.

Contraindicated in tuberculous infections of the eye and in herpes simplex.

How supplied.—Dropper bottle, 2.5 c.c.

Hydrocortisone — Neomycin — ocular therapy: NEO-CORPHOS (Pr), Crookes-Barnes

Description.—A true solution of neomycin sulfate in combination with hydrocortisone-21-phosphate.

Indications.—For ophthalmic inflammation complicated by infection.

Administration.—1 or 2 drops in the eye every 2 hours during the day.

Contraindicated in tuberculous or fungal infections of the eye and in herpes simplex.

How supplied.—Dropper bottle, 5 c.c.

Dexamethasone — Orphenadrine — A.S.A.: DELENAR (Pr), Schering

Description.—Each tablet contains: Deronil (dexamethasone) 0.15 mg., orphenadrine HCl 15.0 mg., acetylsalicylic acid (as aluminum salt) 300 mg.

Indications.—To relieve inflammation, muscle spasm and pain in mild to moderate rheumatic and traumatic conditions affecting joints, tendons and soft tissues; e.g. mild rheumatoid arthritis, mild or moderate spondylitis, subacute or interval gout, bursitis, myositis, synovitis.

How supplied.—Bottles of 100.

Prednisone: PRECORT Bitab (Pr), Can. Pharm.

Description.—Each dappled black and pink Bitab contains: prednisone 10 mg.

Indications.—Conditions amenable to corticosteroid therapy such as collagen diseases; allergic conditions; inflammatory eye conditions, etc.

Administration.—One daily.

How supplied.—Bottles of 25, 250 and 500.

Phenylbutazone — Prednisone: STERAZOLIDINE (Pr), Geigy

Description.—Each orange and blue capsule contains: Butazolidin (phenylbutazone) 50 mg., prednisone 1.25 mg., aluminum hydroxide 100 mg., magnesium trisilicate 150 mg., homatropine methylbromide 1.25 mg.

Indications.—Relief of a variety of rheumatic conditions, e.g., rheumatoid arthritis, bursitis, synovitis, and fibrositis.

Administration.—Individualized dosage. In acute therapy, dosage should not exceed 12 capsules on first day and 6 to 8 on succeeding days. Treatment for more than seven days is rarely necessary. If therapy extends beyond one week, daily dosage should not exceed 6 capsules. In chronic therapy, dosage should not exceed 6 capsules daily and dosage must be tapered off gradually to minimum maintenance level at which patient feels reasonably comfortable.

Contraindications: history of peptic ulcer, diverticulosis, cardiac decompensation and œdema, history of blood dyscrasia, tuberculosis, herpes simplex ophthalmica, recovery phase of gastro-intestinal surgery, agitated psychotic states.

How supplied.—Bottles of 30 and 100.

MISCELLANEOUS

Isoproterenol Sulfate: NORISODRINE Syrup with Calcium Iodide, Abbott

Description.—Each 5 ml. teaspoonful contains: Norisodrine sulfate 3 mg., calcium iodide (anhydrous) 150 mg., alcohol 6%, in a honey-mint flavoured syrup.

Indications.—Prophylaxis and treatment of asthmatic attacks, treatment of allergic coughs and bronchitis.

Administration.—Suggested dosage is normally every 4 to 6 hours: age 1 to 3 years, ½ teaspoonful, repeated in 2 hours if necessary; age 3 to 10 years, ½ to 1 teaspoonful, repeated every 30 minutes up to a total of 3 teaspoonfuls; 10 years and over, 1 to 2 teaspoonfuls, with repeated doses of 1 teaspoonful.

Precautions: not to be given to patients intolerant to iodides; to be given with caution in hypertension or other cardiovascular disease. Overdosage may result in symptoms such as dizziness, palpitation, nervousness, and tachycardia. Dosage should be reduced.

How supplied.—16 fl. oz.

Ethylnorepinephrine Hydrochloride Injection: BRONKEPHRINE HYDROCHLORIDE, Carter C.

Description.—Each c.c. contains ethylnorepinephrine [racemic 1-(3,4-dihydroxyphenyl)-2-amino-1-butanol] hydrochloride 2 mg. in an isotonic saline solution with sodium acetone bisulfite 0.2% and chlorobutanol 0.25% as preservatives.

Indications.—For the relief and management of bronchial asthma. Especially valuable in patients who do not respond to other sympathomimetic compounds.

Administration. — Subcutaneously or intramuscularly. Adults: The average dose is 1 c.c. Repeat every four hours as needed. Children: Dosage varies according to age. Usually 0.5 c.c. to 0.8 c.c. is sufficient. In emergencies, may be injected by *slow* intravenous administration given over a period of 7 to 10 minutes in a dosage of 0.5 c.c.

How supplied.—10 c.c. multidose vial.

Unsaturated fatty acids: LENIC H.P. (high potency), Crookes-Barnes

Description.—Capsules of 1 g., providing unsaturated fatty acid glycerides as follows: arachidonic, pentænoic, and hexænoic, 320 mg.; linoleic, 340 mg.; oleic, 200 mg.; saturated fatty acid glycerides, 140 mg.; and mixed tocopherols 1 mg. No sugars are added.

Indications.—To lower blood cholesterol levels; to raise the level of unsaturated fat in the diet.

Administration.—2 capsules 3 times a day after meals.

How supplied.—Bottles of 100.

Vitamin E: VITA-E "800" Gels, Webber

Description.—Soft gelatin capsule containing 300 i.u. vitamin E.

Indications.—Where vitamin E therapy is indicated.

How supplied.—Bottles of 100, 500 and 1000.

D-amphetamine Sulfate — Prochlorperazine: ESKATROL (Pr), S.K.F.

Description.—Each "Spansule" sustained-release capsule contains: dexedrine (d-amphetamine sulfate) 15 mg., prochlorperazine maleate 7.5 mg.

Indications.—For appetite control in management of obesity where emotional problems are a factor.

Administration.—One daily in the morning.

How supplied.—Bottles of 30 and 250.

PENTOTHAL Sodium Ampoules, 6.25 g., 12.5 g. (Pr), Abbott

Description.—Ampoules now available as 6.25 g. and 12.5 g., each in boxes of 25.

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REVIEW ARTICLE

MYCOTIC INFECTIONS COMMON TO MAN AND ANIMALS*

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UNTIL THE ADVENT of the antibiotics, systemic fungal infections were infrequently recognized. Whenever one was diagnosed in this country it was usually looked upon as a strange and not particularly important infection. The introduction of the antibiotics brought about control of most bacterial infections and focused attention on fungal infections. It was not long before it was realized by those concerned that pathogenic fungi become established in the body in a very insidious manner. The clinical characteristics of fungal infections frequently cannot be differentiated from other infections and diseases. It was this similarity that disguised the mycotic infections and promoted the opinion that systemic fungal infections are not important in our climate. These infections are important, as has been repeatedly demonstrated during the last 12 years by the Ontario Department of Health.

We have stated that the antibiotics, by controlling bacterial infections, have focused attention on fungal infections. They sometimes act in another and dangerous way. It has been frequently reported that the continuous use of broad-spectrum antibiotics encourages infection, especially of the gastro-intestinal tract, by that very common fungus, *Candida albicans*.

If the increase in the number of requests for fungal examinations received at the Provincial Laboratory in Toronto is an indication of the awareness of physicians in Ontario, then it can be said that most physicians consider the possibility of fungal infection in establishing a diagnosis. Because of the recent emphasis on veterinary mycology, veterinarians are also including fungi as possible etiological agents in animal diseases.

Systemic human fungal infections that occur most frequently in Ontario, and also occur in animals, include histoplasmosis, North American blastomycosis, cryptococcosis, candidiasis, sporotrichosis, nocardiosis, and aspergillosis. In addition to these systemic infections, superficial infections caused by the zoophilic dermatophytes are isolated regularly from humans during the winter and early spring seasons. It is common knowledge that animals with ringworm are a source of infection either directly by contact or indirectly by contaminating clothing or their surroundings with infectious material. There is still doubt that animals with systemic fungal infections are a significant source of infection for humans. In regard to histoplasmosis, cryptococcosis, nocardiosis and aspergillosis there is now sufficient evidence[1-3] to show conclusively that the fungi are present in soil and on vegetation. These are sources of infection for both humans and animals. The *Blastomyces dermatitidis* that causes North American blastomycosis has never been found in nature. Since the lungs are commonly infected in the systemic form of the infection and the extremities in the cutaneous form, it is generally believed that the source of this fungus also is exogenous.

We shall confine this paper to the fungal infections that are known to occur most frequently in animals.

HISTOPLASMOSIS

Histoplasmosis has been studied more extensively than any of the other systemic fungal infections already mentioned. Since the reports in 1945 and 1946 by Christie and Peterson,[4, 5] which showed a marked correlation between nontuberculous pulmonary calcifications and positive skin tests to histoplasmin, histoplasmosis has attracted a great deal of attention. Most of these infections are the benign asymptomatic type and occasionally the acute epidemic type but the fatal progressive form is rarely seen. Histoplasmosis is caused by *Histoplasma capsulatum*. The fungus infects a variety of animals and has been isolated most frequently from dogs, cats, skunks, mice and rats.[6] Infection in animals may not always be apparent.[7] Histoplasmin sensitivity has been demonstrated in horses, cattle, sheep, swine and a few chickens.[8-10] Since no one has succeeded in infecting chickens with *H. capsulatum*, it is probable that sensitivity to histoplasmin is the result of frequent exposure to the fungus. In the surveys in the endemic areas of Kansas, Iowa and Missouri, reported by Menges,[10] histoplasma was isolated frequently from the soil. The question of the importance of animals in spreading this infection has been studied a great deal. The conclusion that many have reached is that an infected animal is a possible source of infection but it is likely that most infections of man and animals have a common source in nature, probably the soil. It has been demonstrated by several people that the spores of *H. capsulatum* may be present in the atmosphere.

An interesting demonstration was reported by Rooke[11] from the University of Iowa. A continuous recording particle sampler was used and at the time of the report they had found 19 *H. capsulatum* spores. Another report[12] concerned the

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isolation of *H. capsulatum* from the air in a neglected chicken house. This building had been cleaned of chicken droppings and straw by a family of five who contracted histoplasmosis. Many investigators have found a relationship between areas contaminated by chickens and the presence of histoplasma as well as areas on farms protected from the weather, such as in or near a silo, a dirt floor, and inside and under farm buildings.[1, 13-17] The brown bat has been shown by Emmons[18] to establish conditions suitable to support the saprophytic growth of histoplasma. He suggests that they are responsible for the establishing of the histoplasma in certain urban and rural areas. Experiments have shown that *H. capsulatum* will survive at least eight months in sterilized tap water and alternate freezing and thawing.[19] For over 10 years one of us has maintained stock collections of pathogenic fungi in a deep freeze. *Histoplasma capsulatum* has been kept as long as two years successfully at −23 F.°

Since the source of infection for both animals and man appears to be the soil, the possibility that drinking water might contain viable spores of *H. capsulatum* was investigated by Metzler *et al.*[20] of the Kansas State Board of Health. They showed that settling of the natural turbidity or alum coagulum concentrated the majority of the spores in the sediment. A model sand filter did not remove all the spores suspended in the tap water, and its efficiency was not improved by increasing the depth of the sand. To rid drinking water of viable histoplasma spores it is necessary to provide more available chlorine residual than is necessary for bacteria such as enteric bacteria. Metzler and his colleagues determined that, for the water they were using, it was necessary to have 1.8 p.p.m. of free chlorine in order to kill *H. capsulatum* in one hour. Histoplasma seems to occur in dogs more frequently than in other domestic animals. Cole *et al.*[21] report that the fungus infects all systems of the body but most symptoms are referable to the digestive, lymphatic and respiratory systems. A history of chronic cough and dysentery is common and infected animals usually have enlarged mesenteric lymph nodes, anorexia, emaciation, pulmonary nodules by radiography, enlarged liver, and spleen, and ascites. Examination at necropsy will reveal nodules in the viscera, and ulceration of gastric, intestinal and oral mucous membranes.

Prior and Cole[22] report that they succeeded in demonstrating the communicability of histoplasmosis from dog to dog, but did not demonstrate the transmission of histoplasmosis from dog to man.

NORTH AMERICAN BLASTOMYCOSIS

North American blastomycosis is caused by *Blastomyces dermatitidis*. This fungus has never been isolated from nature although from the clinical characteristics of the infection in humans it is suspected that it originates in nature. In the dog[23] North American blastomycosis is a chronic debilitating disease accompanied by depression, and loss of appetite and weight. In the final stages a purulent discharge from the eyes and nose are not uncommon. Pulmonary lesions occur in most cases. The cutaneous lesions seem to begin as papules and develop into pustules which contain a thick grey mucopurulent material. Menges, McClellan and Ausherman[24] report that the most constant findings are enlargement of lymph glands at the bifurcation of the trachea. Difficulty in breathing and chronic cough are believed to be caused by this mass of enlarged glands.

CRYPTOCOCCOSIS

Cryptococcosis is caused by the fungus *Cryptococcus neoformans*. This infection has been known to many as torulosis and the fungus as *Torula histolytica*. These names are no longer used and the infection is generally known as cryptococcosis. Infections occur frequently in humans and sometimes persist for months and even years before causing death. Unlike histoplasmosis, every infection is very serious, and until recently there was little hope of recovery for anyone infected by *C. neoformans*. For many years the source of this fungus was not known. In 1933, a study of isolations of cryptococci from skin and fæces of humans by Benham and Hopkins suggested an endogenous source. It had previously been isolated from milk[25] but no infection could be found in the cows. In 1951, Emmons[26] reported the isolation of *C. neoformans* from soil. In 1952, a severe outbreak of cryptococcal mastitis in a dairy herd in Maryland was reported by Pounden, Amberson and Jaeger,[27] and in 1953, Simon, Nichols and Morse[28] at the University of Wisconsin also reported an outbreak of mastitis in a dairy herd. The origin of infection was not established for the herd in Maryland but it is believed that the outbreak Simon reported resulted from infusion of the udder with a penicillin mixture at the close of the milking period. *Cryptococcus neoformans* has been reported to infect a variety of other animals including the horse, dog, and cat. A review of infection in animals was given by Barron in 1955.[29]

When Emmons first isolated *C. neoformans* from nature in 1951, he noted that the soil from which he made his isolations appeared to be contaminated by pigeons. As a result of this observation Emmons reported, in 1955,[30] the results of his studies of pigeon droppings. In one location in Maryland he found eight of 11 specimens positive and in Virginia 63 of 111 specimens of pigeon nests and droppings positive. These results have been verified by Kao and Schwarz[31] in Cincinnati, and Littman and Schneierson[32] in New York City.

As a result of these investigations it is now well established that *C. neoformans* is commonly found in pigeon droppings. It is also interesting that neither Emmons nor Kao and Schwarz were able to establish infection in pigeons. In view of the fact that this fungus is commonly associated with pigeon droppings, anyone who attempts to clean areas frequented by pigeons should take proper precautions against infection. These would include:

1. The dampening of excreta with a suitable disinfectant.

2. The wearing of suitable face masks, coveralls and gloves by the workmen. It is probable that the difficulties involved in the cleaning of such areas would encourage the municipal authorities to get rid of pigeons as a menace to the public health.

Also, since *C. neoformans* may infect a great variety of farm animals, veterinarians should encourage farmers to drive these birds from farm buildings. In fact, since pigeons do not serve any useful purpose, their elimination would be in the public interest.

The infection in a dog[33] reported from the Ontario Veterinary College in 1955 appeared as a nasal discharge and ulcerations of the skin of the nose. White papules were present on the tongue. Some of these ulcerated. Lesions also appeared on the inner surface of the lips and the mucous membranes of the mouth. The eyes had some discharged purulent material. The dog had a dry cough and the nasal discharge became hæmorrhagic. The coronary borders of the claws were sore and a grey-white fluid appeared on pressure. At necropsy some small firm nodules were found in the lung.

SPOROTRICHOSIS

Sporotrichosis is caused by the fungus *Sporotrichum schencki*. The habitat is believed to be in nature since the fungus has been isolated from soil, wood and plants. Most infections occur among agricultural workers. Occasionally a veterinarian or a person caring for animals becomes infected. This happened in Toronto a few years ago. Such animals as the horse, dog, cat and rodent are susceptible to infection, and human infections may result from contact with animals that are infected or acting as mechanical carriers. In Ontario, most infections are of the localized lymphatic type and result at the point of injury from scratches or punctures by sharp objects. Nothing was heard about sporotrichosis in Ontario until a report[34] was made of a localized lymphatic infection of a florist's assistant in Windsor in 1951. This report attracted general attention and for the next few years sporotrichosis was diagnosed many times. Some of these cases were reported by Hawks.[35] In 1947, a symposium[36] was published by the Transvaal Chamber of Mines, Johannesburg, on an epidemic affecting over 2800 miners in the gold mines of the Witwatersrand. The fungus was found growing on the mine timbers. Some of the cases with which we in the Provincial Laboratories have been associated are the following:

1. A florist's assistant who had been handling sphagnum moss became infected in the wrist.
2. A farmer's wife who assisted in light farm work was infected on the back of the right hand.
3. A hunter cut his hand opening a can of food and became infected.
4. A veterinarian who bathed a cat's paw later was believed to be infected by *Sporotrichum schenki*.
5. A retired man became infected in the hand following the preparation of his garden area for planting.

In humans, infection usually begins on an extremity such as a finger or hand. The primary lesion appears as a hard spherical nodule which becomes black and necrotic. There then appears along the lymphatics a series of raised hard reddened lumps which may bear some resemblance to boils. However, these lesions are cold and not noticeably tender. These nodules also ulcerate and a small amount of purulent material is produced. The lymphatic vessels connecting the nodules become thickened and cord-like.

CANDIDIASIS

Candidiasis is a common infection in man and occurs frequently in animals. In man, the species most commonly pathogenic is *Candida albicans* but in animals other species such as *C. krusei*, *C. parakrusei*, *C. tropicalis* and *C. pseudotropicalis* are important in addition to *C. albicans*. Some know *C. albicans* as *Monilia albicans*. The species in this genus are yeast-like fungi and are present as saprophytes on normal mucous membranes and in fæcal material. It is, therefore, to be expected that these fungi would be found contaminating stables and areas frequented by animals, and ready to cause an infection when conditions became suitable. Infections in animals may cause lesions in the oral cavity and œsophagus, and skin infection of the young resembling thrush in humans. Many cases of otitis externa of dogs are caused by species of Candida. Within recent years infections of the bovine udder by *C. krusei*, *C. parakrusei*, *C. albicans*, *C. tropicalis* and *C. pseudotropicalis* have been recorded. Infection is characterized by a swollen gland, thick milk and fever. Antibiotic treatment, except perhaps with nystatin, is of no value. The organism will disappear from the gland in three or four weeks when aided by frequent milking. The organism may be introduced into the gland when antibiotic treatment for a bacterial infection is given.

NOCARDIOSIS

The infection nocardiosis is caused by aerobic actinomycetes, usually *Nocardia asteroides*. In man,

this fungus may cause a chronic infection of the subcutaneous tissues or a pulmonary infection that simulates tuberculosis. The fungus may be carried from the lungs to other parts of the body, especially to the brain. *Nocardia asteroides* may infect animals also. Infection of the dog in Canada has been reported by Archibald,[37] Barnum and Fuller,[38] and Ditchfield, Butas and Julian.[39] Pier, Gray and Fossatti[40] recorded isolation of species of nocardia from bovine mammary gland infections. The mastitis is characterized by abnormal secretion and marked fibrosis. Treatment has been unsuccessful.

ASPERGILLOSIS

Some of the commonest fungi found in soil and on vegetation are species of aspergillus. A few of these species infect man and animals. *Aspergillus fumigatus* is the species usually incriminated. Although infection by these fungi is occasionally established in man, aspergillosis is primarily an animal infection. There is an apparent increase in its occurrence in chicks where it has been isolated from organs other than the lungs and air sacs. Aspergilli, especially *A. fumigatus*, have been the cause of bovine abortion. It is an infection of the placenta and the organisms are found in the stomach contents of the fetus in 25% of the cases and cause skin lesions in only 5%.

FUNGAL INFECTIONS OF HAIR, SKIN AND NAILS

The fungal infections of the hair, skin and nails in humans are a perennial problem, and infection from animals usually increases during the winter and early spring. The fungi that cause human infections are divided into three groups: the human types, the animal types, and the soil types. Since our interests here are in fungal infections common to man and animals, we are chiefly concerned with the animal types. In the animal group are the following fungi of interest to us: *Microsporum canis, Trichophyton mentagrophytes,* and *Trichophyton verrucosum.* Infections caused by the last species usually increase during the late winter and early spring. It is the common cause of ringworm in cattle.

Microsporum canis infects chiefly cats and dogs. Infections by this fungus in an animal spread quickly to children who are in contact with the infected animal and then to other children, usually playmates or children in direct contact. Small epidemics occur in this way but large epidemics such as are caused by *M. audouini* do not occur. It has been established by Kaplan *et al.*[41] at the Communicable Disease Center, Atlanta, Georgia, that cats under one year of age are more frequently infected. It is important to know that not all microsporum-infected cat hairs fluoresce; Kaplan *et al.* report that only 30% of hairs infected by *M. canis* show fluorescence. In such instances when a cat is suspected of being infected but no fluorescence can be demonstrated with the Wood's ultraviolet lamp, specimens of hair should be collected from suspicious areas for laboratory study. Lesions in cats occur principally on the head and extremities and are influenced by the age of the cat. In kittens, infection may spread over the entire body, with scattered loss of hair and scaling. Infection in adult cats may be barely noticeable and appears as scattered patches over the face and paws or as loss of hair along the edges of the ears.[42] Infection in the dog is usually more easily seen. There is commonly a loss of hair in circular patches, especially on the head and extremities. Most infections occur in young dogs. Some believe[41] that *M. canis* loses its infectivity after a few human transfers and that this is the reason why it does not cause large epidemics among children.

TRICHOPHYTON VERRUCOSUM

Trichophyton verrucosum is the principal cause of ringworm in cattle in the United States and it is the fungus we expect to isolate when the dermatologist reports that the patient has been in contact with cattle showing ringworm-like lesions. Infection is more common in calves and is most common during the winter and early spring when cattle are kept in barns. The lesions are frequently circular, raised and crusty, and are found usually on the head, around the eyes and mouth, and at the base of the tail. The age of the animal seems to have an influence on the degree of infection, younger animals frequently showing the more extensive and severe infections. Human infections by *T. verrucosum* may result from direct contact with infected cattle or indirectly from something contaminated by an infected animal. Rook and Frain-Bell[43] in England report infection in a child who had placed a calf's chain around her own neck. They believed that other children had picked up the infection from posts and trees against which the cattle had rubbed. Georg, Hand and Menges[44] report that a pre-existing skin lesion may provide a favourable condition for infection by *T. verrucosum.* They report infection in lesions of allergic eczema and an acid burn. Infection in humans usually occurs on exposed areas, especially the scalp and beard areas where it usually causes suppurative lesions.

TRICHOPHYTON MENTAGROPHYTES

Trichophyton mentagrophytes is one of the commonest dermatophytes isolated from humans. Most isolations are from foot scrapings but isolations are also made from other parts of the body, especially the face, neck, scalp and arms. In a survey of suppurative ringworm in rural Michigan[44] half of the infections were caused by *T. mentagrophytes.* Most of these infections could not be traced to infected cattle. In the same year Georg[42] also re-

ported that *T. mentagrophytes* is frequently isolated from rats, mice, rabbits, chinchillas, guinea pigs, dogs and other small animals. These animals may act as carriers and have no visible signs of infection. It is pointed out that these small animals, especially rats and mice, may contaminate areas of the farm buildings with infected hairs and scales. It is probable that the fungus would survive for long periods, especially in dry areas, and be a source of infection for both animals and man. We have demonstrated, in our paper outfits supplied to physicians for submission of specimens to the laboratory, that *M. audouini* will remain viable in hair and skin scrapings for as long as two years. These specimens were kept dry and the temperature ranged from about 70 to 100° F.

Concluding Remarks

In conclusion, fungal infections may be divided into two groups, superficial and systemic. It is generally known that the zoophilic dermatophytes that cause superficial infections spread from animals to man. In regard to many of the systemic infections, the facts suggest that infections in man and animals have a common source in nature in soil, bird droppings and vegetation. Measures should be instituted in the interests of the public health to locate and eliminate such areas of infection.

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GENERAL PRACTICE

TIMING OF OPERATIONS IN PÆDIATRIC SURGERY

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Introduction

In this presentation conditions of an emergency nature will not be included and only elective surgical procedures will be considered. The conditions to be discussed are those most frequently seen in daily practice.

The timing of surgical procedures is recognized as being of considerable importance in every branch of surgery. This is especially true of pædiatric surgery where the eventual result of the treatment often depends almost as much on when a condition is treated as on how it is treated.

The views to be given are those of the surgical staff of The Montreal Children's Hospital and not solely of the authors of this paper.

In planning the treatment of any infant or child, the surgeon must find answers to the following questions:

1. When will this child be best equipped to withstand the surgical and psychic trauma of the proposed operative procedure?

2. When will the anatomic development of the involved structures offer the best chance for successful surgery?

If the answers to these two questions indicate that a waiting period is desirable, then a third question must be considered:

3. What complications may arise because of the delay?

The answers to these questions must be carefully assessed by the surgeon if the most rational plan of treatment is to be chosen.

A decision on timing involves a conscious or unconscious consideration of numerous factors, many of which are peculiar to pædiatric surgery,

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especially when the very young are involved. These factors will first be presented in a general manner as they apply to all pædiatric surgical problems, after which some of the more commonly seen conditions will be considered, with emphasis on the factors involved in the selection of the most appropriate time for surgical intervention.

General Principles

1. *The Child Must be Free from Infectious Disease*

Perhaps it is unnecessary to mention this self-evident fact, but, apart from any adverse effects the infectious disease may have on how the child will tolerate anæsthesia and surgical intervention, the rapidity with which the communicable diseases spread among children in hospital justifies its inclusion among the general principles.

2. *Age and Size of the Patient*

No hard and fast answer can be given regarding the question of the age at which it is safe to perform an elective operation on an infant, but at The Montreal Children's Hospital we believe that an infant becomes a reasonable risk for any elective surgery when it weighs 10 lb. and is gaining. This is only true, however, if anæsthetists are available who, by virtue of their experience, are familiar with the problems that can arise during the operative and postoperative phases of treatment. With less favourable conditions a longer delay would clearly be necessary, and the plan of treatment must depend, therefore, on the specific circumstances.

3. *Co-operation of the Patient*

The success of many surgical procedures requires considerable co-operation on the part of the patient during the period of recovery and rehabilitation. This is especially so in the fields of orthopædic and plastic surgery. When this is the all-important factor, it is wise to delay the operative procedure until the patient is about four years of age, at which time such co-operation can be anticipated.

4. *Limitation of Psychic Trauma*

Any surgical procedure on a child involves a degree of psychic trauma. The extent of this can be minimized only by careful planning. No child should be admitted to hospital, except under emergency conditions, until everything possible has been done to prepare him for hospital stay. The child should be informed of everything that is going to happen to him, within the limit of his capacity to understand. Explanations can be given in simple terms, and surprises should be avoided as much as is possible.

If at all possible, hospitalization should be avoided during periods of emotional stress in the home. Hospitalization at such a time is likely to be interpreted as a form of punishment. We are informed by the psychiatrists that any surgical procedure undertaken then can be interpreted as castration. The emotional aspect assumes its greatest importance in the age-group two to four years, that is, during the period when a child is old enough to miss his home and family but too young to understand why such separation is necessary.

Specific Elective Procedures

1. *Inguinal hernia.*—The infant with an inguinal hernia is accepted for elective repair when a weight of 10 lb. has been reached or as soon thereafter as it occurs. The high incidence of strangulation and the possible danger of testicular or bowel damage produced by waiting, far outweigh any consideration that can be given to the rare spontaneous cure. This opinion, however, takes into consideration the fact that in the great majority of cases only a simple excision of the sac is performed as opposed to formal repair of any weakened inguinal canal musculature. It is an extremely simple surgical procedure that can be tolerated by any healthy infant or child without danger of testicular damage. The opinion that these hernias should not be repaired until the child is four, five or six years of age originated when formal repairs were being carried out and in these circumstances the additional dissections too often damaged the tiny testicular vessels of the infant.

2. *Umbilical hernia.*—These should not be repaired before two years of age since the great majority will disappear spontaneously during these two years. Rarely, a very large umbilical hernia will require operative repair at an earlier age. It has been stated that an umbilical hernia never strangulates, but this statement is not true.

Spontaneous cure can often be hastened by appropriate adhesive strapping designed to approximate the rectus muscles. The use of a coin with adhesive strapping has been advised by some. This method, although keeping the hernia reduced, is undesirable since it also holds the rectus muscles apart.

3. *Hydrocele.*—The majority of hydroceles of infancy disappear during the first year of life. If persistent after this time, excision is recommended and at operation a search is also made for the presence of any hernial sac. The massive hydroceles that are seen occasionally may need operation earlier, 10 lb. in weight and gaining again being the time factor consideration.

4. *Anal fissures.*—The acute anal fissure is very rarely a surgical problem. In our experience it can be cured almost invariably by a conservative regimen consisting of daily digital dilatations by the mother, a laxative diet, and a local anæsthetic ointment.

In chronic cases, however, where there is deep induration and the edges of the fissure are rolled and cicatrized, excision of the fissure and division of the subcutaneous sphincter ani is necessary.

5. *Hæmangioma.*—Over 1000 patients with hæmangiomata are being followed up at present at The Montreal Children's Hospital. Experience gained from this study, together with figures emanating from other centres, indicates that approximately 92% of these lesions disappear spontaneously. Therefore, the attitude has been adopted that most hæmangiomata do not require treatment.

Hæmangiomata involving the eyelids, alæ nasi and ears, however, are more of a problem and may need early excision. Although these too will usually disappear in time, too often they do so only after destroying underlying cartilage, which necessitates complicated reconstructive procedures.

Hæmangiomata about the lips have a very poor reputation for disappearing spontaneously, and for this reason should be excised early. Those of the lower lip can usually be excised with little or no residual deformity and seldom present a problem. Those of the upper lip present much more difficulty, a good cosmetic result being difficult to attain. If the lesion involving the upper lip is a static one, a better result can be anticipated if excision is delayed until after four years of age.

Excision is recommended for hæmangiomata in the diaper area. Soiling by urine and fæces causes a chronic irritation which produces ulceration, infection and bleeding, all of which are avoided by early excision.

If any hæmangioma shows no signs of regression after several months' observation, the natural process of regression can usually be initiated by a minimal dose of irradiation. The "port wine stains", of course, are excluded from this category of spontaneous cure, since they are there for life.

6. *Cleft lip.*—These defects can be repaired at any time during the postnatal period. The policy followed at The Montreal Children's Hospital is to undertake operative repair when the infant weighs 10 lb. and is gaining. This has the advantage of allowing time for the recognition of any other congenital anomaly that may be present.

7. *Cleft palate.*—Repair of these defects requires careful timing. In general, the incomplete clefts are repaired at about 16 months of age. This delay allows a period during which maximum growth may occur without running the risk of the development of poor speech habits which create problems at a later date both for the child and the speech therapist.

Where the cleft is complete with a split alveolus, it is recommended that one await the stabilization of the defect, i.e. wait until no further spontaneous narrowing of the cleft is occurring and accept, if necessary, the development of poor speech habits. Stabilization of these defects will usually be observed between 18 months and three years of age.

8. *Syndactylism.*—The important limiting factor in the timing of the operative repair of this condition is the amount of co-operation that the patient is able to give during the period of rehabilitation. This, however, must be correlated with the anatomic structural defect.

Where the web is loose and composed of skin and subcutaneous tissue only, the repair is best undertaken in the immediate pre-school period as it is obviously desirable to have the repair completed by the time the child reaches school age.

Where bony and/or joint fusion exists, one cannot take advantage of so long a delay. The fingers in the newborn are of approximately the same length, but around two years of age, the third finger starts to grow more rapidly than its neighbours. Therefore, repair should be performed before this happens, to avoid growth distortions which may affect the ultimate result of the operation.

9. *Hypospadias.*—The size of the penis, depending on age, is a limiting factor in the operative repair of the condition, and good timing demands waiting until anatomic growth of the penis renders surgery more easily accomplished. On the other hand, for psychological reasons, the defect should be repaired before the child reaches school age. If a chordee is present it should be divided at about two years of age to prevent interference with penile growth.

10. *Extrophy of the bladder.*—On the basis of a fairly limited experience, it is now believed that repair of the defect is preferable to excision of the bladder with implantation of the ureters into the bowel. The repair is a staged procedure in which bilateral ilial osteotomy, allowing approximation of the two halves of the pubis, is followed at a second stage by closure of the bladder and repair of the hypospadias.

The anatomical size of the involved structures is the important consideration in timing, and it is felt that the average six-month-old baby is big enough to make this procedure practical. The development of squamous metaplasia in the bladder mucosa makes the repair more urgent, especially in the female where the operation is less difficult and it, therefore, becomes less necessary to await growth.

Should the repair be unsuccessful in that no functioning sphincter results, the construction of an ileal bladder can still be performed with little lost. When the procedure is successful, it is believed that the result in terms of damage to the upper urinary tract will be vastly superior to anything achieved in the past.

11. *Cryptorchidism.*—The timing of operative intervention in cryptorchidism is a rather controversial subject. The majority opinion held at The Montreal Children's Hospital is that the undescended testis, especially if bilateral, should be brought down into the scrotum at about eight years of age and certainly before the age of 10 years. The rationale for doing so is based on biopsy findings. Testicular biopsies performed on testes that have descended or have been brought down after 10 years of age are usually reported as showing changes compatible with loss of fertility.

12. *Club feet.*—It is important to point out that most orthopædic problems in infancy and childhood can be much more simply handled if recognized and treated early. In many cases early recognition makes the difference between a good result obtained by conservative therapy and an equivocal result reached after extensive surgical intervention.

Applying these principles to club feet, we believe that these are best handled by vigorous non-operative treatment starting as soon after birth as possible. The objective should be rapid correction by manipulation. It is important to realize, however, that if such a regimen is not producing results rapidly enough, surgical intervention may become necessary, even in the first year of life, to prevent the deformity from becoming fixed. For

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example, if the talus is left too long in the equinus position, no amount of heel-cord lengthening will make it fit back into the ankle mortise.

13. *Congenital dislocation of hips.*—What has been said above regarding the general principles of treatment in orthopædic anomalies applies equally to dislocation of the hips as to club feet. Here again the whole plan should be directed at getting treatment started early when conservative measures offer the best chance of a good result. When open reduction becomes necessary, the results are not always good.

SUMMARY

The general principles of the timing of surgical intervention in elective pædiatric surgical conditions and their application in certain specific conditions have been presented.

PUBLIC HEALTH

SURVEILLANCE REPORTS OF EPIDEMIC OR UNUSUAL COMMUNICABLE DISEASES

INFLUENZA

During the first three weeks of January, about 30% of the high-school population of Qualicum, British Columbia, suffered from an influenza-like illness.

UPPER RESPIRATORY INFECTION

In *Manitoba* there has been considerable upper respiratory disease associated with fever, sore throat, "head cold" and occasionally pneumonitis simulating mild influenza. Most disease has been seen in children under five years of age but persons up to 60 years have been affected. From 10 patients, adenovirus type 3 and from one patient adenovirus type 1 were isolated during December 1959 and January 1960. In addition, six patients have shown an increase in antibodies to the adenovirus by the complement-fixation test. Since October 1959, five deaths have occurred in children under 19 months of age, in whom an interstitial pneumonitis was demonstrated at autopsy. Adenovirus type 3 was isolated from the lungs in all of the cases. There has been no laboratory evidence of influenza in the community.

MUMPS

Twelve cases of mumps have been reported during January from Camp Shilo, Rivers, Manitoba.

TYPHOID FEVER

One case of typhoid fever has been reported from Eskimo Point, Northwest Territories.

GASTRO-ENTERITIS

An outbreak of a severe form of enteritis, with two fatalities, has occurred at St. Paul, Alberta, about 135 miles north-east of Edmonton. About 15 cases have been admitted to hospital and it is estimated that three or four times as many are at large. It has affected all ages, children under one year being the worst affected. The onset is sudden, with diarrhœa, vomiting, fever and rapid dehydration. The illness lasts four to five days and has a tendency to relapse. The two deaths were in infants ten months old. The enteritis has not responded to antibiotics or chemotherapy. The source of the infection has not been traced and no organism has been obtained on culture.

ORNITHOSIS

A case of ornithosis has been reported in an adult female in New Brunswick.

International Reports

INFLUENZA

United States.—Scattered, limited outbreaks of influenza-like disease are still being reported. Many of the outbreaks reported this week are in states in the south-eastern United States. The number of outbreaks reported from other areas is declining. Clinical influenza remains widespread in Texas but appears to be subsiding gradually in southern California.

An increased incidence of febrile respiratory disease and local outbreaks of clinical influenza has been reported in a total of 35 states. Type A2 influenza virus has been isolated in a total of 22 states, including the District of Columbia.

There has been no indication of a widespread occurrence of influenza-like illness in the north-eastern part of the country. The reported outbreaks continue to be localized. Absenteeism in schools and industries most affected by the disease has not exceeded 15 to 20%.

Europe.—A number of sporadic cases apparently due to the influenza A2 virus have appeared in schools, hospitals, prisons, and military establishments in Italy, Switzerland, the Federal Republic of Germany, Denmark, the Netherlands, and France, and there have been sporadic cases due to influenza B virus in similar communities in Italy and Finland. None of these influenza-like outbreaks have proved, so far, to be nearly as widespread as during the pandemic of 1957-58. The disease is generally benign and of short duration.

United Kingdom.—The British Ministry of Health commented that there is no indication that influenza is prevalent in England and Wales, and there have been no laboratory isolations of either the influenza A2 or the influenza B virus.

Epidemiology Division, Department of
National Health and Welfare,
Ottawa.

February 13, 1960.

LETTERS TO THE EDITOR

CANCER AND SMOKING

To the Editor:

The article "Cigarette smoking and lung cancer in Canada" by E. C. Hammond and E. L. Wynder (82: 372, 1960) is of interest. No mention is made of the immunity aspect of lung cancer.

In this regard I fail to rid myself of what appears to be a pertinent observation. "If a person is immune, he will not get cancer; if he is susceptible, any factor may trigger it."

I greatly doubt, if it were possible to eliminate cigarettes, that it would appreciably change the various charts or graphs shown in the article.

OSWALD W. ANDERSON, M.D.

Bancroft, Ont.,
February 15, 1960.

WHAT IS AN "R.T."?

To the Editor:

We wish to call the attention of the members of the Canadian Medical Association to the fact that there is an organization calling itself "American Radiography Technologists" which has been admitting to membership so-called technicians and authorizing them to use the designation "R.T."

Persons so designated should not be confused with the R.T.'s recognized by the American Registry of X-Ray Technicians and the Canadian Society of Radiological Technicians; they will not be granted reciprocal membership in Canada.

The Canadian Society of Radiological Technicians, whose executive secretary is Mrs. E. I. Hood, R.N., R.T., 2175 West 16th Avenue, Vancouver, B.C., is the sole organization in Canada offering certification or registration of x-ray technicians recognized by the Canadian Medical Association and the Canadian Association of Radiologists. The C.S.R.T. offers an opportunity for examination after the technician has followed a course of training approved by the Joint Council on Technical Training of the C.A.R. and C.S.R.T. Students who have passed this examination may be registered in the C.S.R.T. Registry and thereupon are authorized to use the designation "R.T." The C.S.R.T. has the reciprocal agreement with the American Registry of X-Ray Technicians whereby students who have qualified in a similar way and become registered in the United States may receive their Canadian R.T. by reciprocity, upon application and payment of a nominal fee.

It is the considered opinion of the Joint Council on Technical Training of the C.A.R. and C.S.R.T. that the designation "R.T." has in the eyes of the medical profession, x-ray technicians, hospital personnel and the public acquired a definite meaning signifying the successful undertaking of a given course of training, a specific level of achievement, adherence to a well-defined code of conduct and passing of a supervised examination.

I. R. FISHER, R.T., President,
Canadian Society of
Radiological Technicians,

New Mount Sinai Hospital,
Toronto, Ontario,
February 20, 1960.

"WE WISH WE HAD WRITTEN THAT"

To the Editor:

I do not know if this will qualify for your items "We wish we had written that" because the words were spoken and not written, but I always remember with pleasure some of the opening remarks of my old teacher, Sir Robert Hutchison, in his course of lectures on therapeutics. "Now abideth, diagnosis which is largely a matter of faith, prognosis which is largely a matter of hope, and treatment which is largely a matter of charity and I may add, that the greatest of these is charity."

J. E. L. BENDOR-SAMUEL, M.B.,
D.O.M.S.

St. Mary's and Vaughan,
Winnipeg 1, Manitoba,
February 3, 1960.

To the Editor:

Times change maybe less than we think. A woman patient once asked Dr. Bouvart (1711-1787) about a new medicine which was very much in vogue at the time. "Very good," he replied, "but take it quickly, while it is still worth something."

F. J. MORAN, M.D.

Bobcaygeon, Ont.,
February 7, 1960.

CERTIFICATION EXAMINATIONS OF THE ROYAL COLLEGE

To the Editor:

The Council of the Royal College of Physicians and Surgeons of Canada has instituted a regulation which states that in 1960 and thereafter, candidates for the Certification examinations of the Royal College must be Licentiates of the Medical Council of Canada or possess a licence to practise in one of the provinces of Canada.

This regulation will not apply to eligibility for the Fellowship examinations.

JAMES H. GRAHAM, F.R.C.P.[C],
The Royal College of
Physicians and Surgeons
of Canada,
74 Stanley Avenue,
Ottawa 2, Ontario,
February 12, 1960.

PROVINCIAL NEWS

SASKATCHEWAN

The Saskatchewan Hospital Association, in a recent news release, stated that it was in favour of the principle of prepaid medical care. At the same time the statement said that the Association was keenly aware of the fact that hospitals in Saskatchewan would be closely involved in any province-wide medical-care plan and, therefore, the Saskatchewan Hospital Association was of the opinion that it should be represented on any committee set up to develop a province-wide medical-care plan.

The statement also noted that the Association was not voicing approval of the C.C.F.'s compulsory medical-care plan.

The city of Moose Jaw has been asked by the city of Prince Albert to join in a move to press the Provincial Government for immediate action to relieve municipalities of some of the burden of medical care of indigents.

In its submission the background of the problem was outlined. At the request of the Provincial Government the committee of the Saskatchewan Urban Municipalities Association worked with a committee of the Saskatchewan Association of Rural Municipalities and the Welfare Department of the Provincial Government to provide a new setting for the administration of social aid effective April 1, 1959.

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Under that arrangement the government was committed for a larger percentage of social aid, but the municipalities assumed the burden of administration and health care of a large group of people who had formerly been the responsibility of the Provincial Government.

At the time of the committee's work it was known that the arrangement would work to the disadvantage of the municipalities unless some new arrangement were made with the Health Department for sharing the health-care costs. It is understood that the committee undertook to accept the Social Aid Act on the understanding that no time would be lost in working out the sharing of these costs, and on that understanding only.

Premier Douglas in a recent news release has stated that the C.C.F. Government's Advisory Committee on its proposed compulsory prepaid medical-care scheme will be given a free hand. A proposal of the committee's set-up had been sent to the College of Physicians and Surgeons of Saskatchewan. They had recommended a number of changes. Mr. Douglas also said that the Government is in favour of these changes but declined to say what the suggested changes are or to outline the draft. He further stated there would be no compulsion for the committee's members to accept any government suggestions.

During February, Saskatchewan's Liberal Leader, Ross Thatcher, outlined his party's answer to the C.C.F. Government's prepaid compulsory medical-care plan.

If elected in the provincial election, expected this spring, Mr. Thatcher stated that the Liberals would sponsor a private enterprise scheme similar to the doctor-sponsored ones in operation already. Mr. Thatcher said, "We believe there is need for such extended medical services, particularly to take care of what might be termed catastrophic or large medical bills."

Mr. Thatcher said that the Liberal Party believes the problem can be met most economically by a province-wide medical insurance plan similar to that presently operated by Medical Services Incorporated or Group Medical Services.

Professor G. J. Fraenkel, professor of surgery, University of Otago, New Zealand, visited the Medical School in Saskatoon during February. While here he spoke on "Some non-malignant lesions of the colon".

Group Medical Services of Regina reported a surplus of $5500 on its 1959 operations. Now in its 11th year of operation, the non-profit doctor-sponsored medical plan has 68,200 members. It was reported that subscriber rates have remained unchanged since 1957 because of the sound financial position of the Association.

Regina General Hospital has announced a new student nurse training program similar to some in operation in Eastern Canada. The program calls for two years' training in basic theory and supervised practice in hospital, followed by a year of internship. Students will not be expected to carry any responsibility for services in the first two years of the course, which is expected to go into effect in September of 1960.

Dr. T. E. Hunt of Saskatoon was elected president of the newly organized Co-ordinating Council on Rehabilitation of Saskatchewan at the recent conference of more than 40 voluntary and governmental agencies. Dr. A. E. Buckwold of Saskatoon was named president-elect. A new organization has been formed to improve and expand services available to disabled persons and to encourage research in various rehabilitation areas.

Regina General Hospital is planning an expansion program to increase the hospital's capacity to 1000 beds.

Dr. Lawrence J. Peters, professor and head of the department of pharmacology at the University of Kansas and Editor of the *Journal of Pharmacology & Therapeutics*, lectured at the Medical Conference in the University Hospital on the chlorothiazide diuretics and discussed the current investigation of drugs by the Special Committee of the U.S. Senate. Dr. Peters is a native of Saskatoon and a graduate of the University of Saskatchewan in Pharmacy. He took his Ph.D. at the University of Minnesota and M.D. at Western Reserve University, Cleveland. At the latter medical school he participated in the curriculum revision which has had a wide influence in medical education planning.

Dr. H. B. Atlee, professor emeritus of obstetrics and gynæcology, Dalhousie University, visited the University Hospital and Medical College February 1-2, taking part in the departmental teaching, meeting with members of the Committee on Studies and addressing the student body on "Medical education and medical practice as I see it".

Saskatchewan dentists will ask for amendments to the Dental Profession Act when the Legislature convenes in February. The proposed amendments will cover several points, and among them are the definition of dentistry, deletion of the "Oral Health Certificate" clause, and the inclusion of a new clause requiring prescriptions from dentists for false teeth. Clarification of the definition of dentistry is being requested so that only fully trained university graduates in dentistry may practise in Saskatchewan. The Dental College feels that the present wording of the Act permits unqualified persons to engage in almost any type of dentistry except extractions.

G. W. PEACOCK

QUEBEC

The government in power of the provincial legislature introduced on January 27 of this year Bill No. 66 which is a measure entitled "An Act Respecting Hospitalization Insurance". This bill was introduced by the Minister of Health, the Hon. Dr. Arthur Leclerc, and it is understood that the bill is an authorization to enable the government to set up an independent commission whose functions will be "to investigate hospitalization problems in the province with a view to adoption of a hospitalization insurance plan." This body is to be known as the Health Insurance Inquiry Commission and will consist of not less than five or more than seven commissionaires who will be able to call upon various experts, specialists and technical advisers. It is understood that the board's findings and recommendations are to be submitted not later than December 1 of this year. It is obvious that the com-

position of the commission will clearly require the most careful consideration. It is certainly desirable to have it as representative as possible of the provincial community. Since the commissionaires may summon as witnesses any number of provincial minds and benefit from any amount of medical opinion, the membership of the commission should embrace persons who will be in a position at all times to view the question of health insurance schemes in its widest application. It is the hope of every member of our Division, I am sure, that with such a balance and such a broad approach, useful results will be forthcoming on this problem of such far-reaching import to the people of this province.

On February 1, the Montreal Medico-Chirurgical Society presented a symposium on rheumatoid arthritis at the Queen Mary Veterans Hospital. Dr. John R. Martin, chief of rheumatology at the Montreal General Hospital, acted as moderator and Dr. Louis Johnson of the Royal Victoria Hospital, Dr. de Guise Vaillancourt of the Hôtel-Dieu and Dr. Anthony Sowden of the Royal Victoria Hospital and the Rehabilitation and Physiotherapy Institute were the panelists. Dr. Martin introduced the panel and outlined the present status of rheumatoid arthritis in Canada. Dr. Johnson reviewed the clinical aspects of this disease process in regard to diagnostic aids, particularly early symptoms and signs. He stressed the problems in differential diagnosis which can at times be very difficult and complications which may arise. Then Dr. Martin briefly outlined the laboratory aids that are available and what is known of the physiological and pathological process in this disease. It would seem that of all the tests available the RA factor (latex modification) probably gives the greatest assistance. It is positive in 70% of patients, but has a tendency to become positive somewhat late in the disease. All laboratory tests are of some aid if used judiciously, but none are really specific tests. He stressed the need for further studies. Dr. Vaillancourt reviewed the management of the patient with rheumatoid arthritis. It is most important that the patient be told all reasonable information about the disease. Rest and controlled physical activity are of primary importance. In regard to drug therapy, it is important that the physician have a thorough understanding of the advantages and disadvantages of each preparation. Steroids should never be used alone, but only with other appropriate therapy such as rest, controlled physiotherapy and rehabilitation. Dr. Sowden gave an excellent outline of the physiotherapy and rehabilitation aids that are available and that should be utilized to their full extent; emphasis is on prevention of disability, restoration of function, reestablishment of independence and vocational resettlement.

On February 11, the School of Nursing of the Montreal General Hospital announced two innovations destined to promote closer liaison between staff, students and the parents of students. One is the formation of the Montreal General Hospital School of Nursing Associates, an organization comprising parents or guardians of students in the school. The second is the establishment of the mentor system under which the students in groups of four are assigned to a member of the staff who acts as their mentor. The main purpose of the School of Nursing Associates is to keep its members and the general public informed of the aims and objectives of the school with a view to providing a better understanding of the nursing profession and to aid in promoting the interests of the school. On a longer-term basis, the Associates aim to provide bursary assistance to needy students. The mentor system is a means of combating the disadvantages of large numbers, the chief of which is an atmosphere of impersonality.

A. H. NEUFELD

NOVA SCOTIA

Dr. Kurt Aterman, associate professor of pathology at Dalhousie University and pathologist at the Children's Hospital in Halifax, has been awarded a Doctor of Philosophy degree, in absentia, from the University of Birmingham. Dr. Aterman holds a degree of Doctor of Medicine from the University of Prague and has received honors in medicine and a child health diploma from Queen's University, Belfast. He is a veteran of the Royal Army Medical Corps, with service in India, and is a member of the Royal College of Physicians of London.

Dr. Aterman is the author of a number of papers on pathological subjects, several of which have been published since he joined the Dalhousie staff in 1958.

At a recent meeting of the Nova Scotia Heart Foundation, Mr. A. B. Hill, Toronto, President and Chairman of the National Heart Foundation, stated that diseases of the heart and blood vessels accounted for more deaths and disability than all other serious diseases of mankind. Mr. Hill said that the statistics for 1959 showed that more than 66,000 Canadians died of heart disease, and more than 250,000 were disabled because of heart disease. Because of these facts, immediate financial help is urged for heart research.

On the financial side he stated that more than $100,000,000 was lost in direct income by its victims, and about $150,000,000 was the conservative total cost of care and treatment of patients. More than 49% of all deaths of men between 40 and 54 years were due to heart disease. The objective of this year's campaign is $1,242,000, or eight cents per capita.

There are in Canada good research programs, particularly in the cities of Halifax, Montreal, Toronto, Saskatoon, Edmonton, Winnipeg and Vancouver, and Canadian heart research compares favourably with that of any country, and indeed is ahead of many. Mr. Hill further stated that the Heart Foundation of Canada provides fellowships and grants-in-aid in the field of heart research to all Canadian medical schools, teaching hospitals and clinical investigation centres. In addition to these projects he said top-ranking medical authorities have estimated that at least 30 more full-time doctors could be employed at once on cardiovascular research.

Dr. Lea C. Steeves of Halifax, executive member of the National Heart Foundation, and Mr. Hill, chaired the meeting.

Dr. Basil Kenneth Coady, graduate of Dalhousie in 1938, has been appointed surgeon-in-chief, Surgery B, at the Victoria General Hospital. Dr. Coady is a native Nova Scotian. After his graduation from Dalhousie he took three years in surgery at the Crile Clinic in Cleveland. He served during most of World War II in the Royal Canadian Navy as Naval Surgeon.

W. K. HOUSE

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ABSTRACTS *from current literature*

MEDICINE

Pulmonary Alveolar Proteinosis.

F. B. LANDIS, H. D. ROSE AND R. O. STERNLIEB: *Am. Rev. Respiratory Dis.*, 80: 249, 1959.

Pulmonary alveolar proteinosis occurs chiefly in adults and is characterized by insidious onset, slow progression, cough, increasing fatigue, chest pain, dyspnœa and weight loss. The first manifestation is often a febrile illness, but fever is usually slight or absent during the prolonged clinical course. The typical roentgenographic picture consists of a bilateral peri-hilar butterfly infiltration, simulating pulmonary œdema. The pulmonary lesions detected roentgenographically may persist for months or years; may clear, remain stationary, or progress. The etiology is unknown, but since the lung appears to be the primary site of involvement, noxious inhalants have been suspected.

A case is reported that presents several interesting features. Thrombophlebitis, not previously reported in association with proteinosis, recurred on three occasions. The presence of thrombophlebitis, pulmonary symptoms and infiltrates in the lower lung fields strongly suggested pulmonary infarction, and probably delayed establishment of the correct diagnosis. The significance of thrombophlebitis occurring in a patient with proteinosis is unknown; it may have been coincidence. There were also unexplained laboratory findings, including elevated serum lipid and total cholesterol levels, hyperglobulinæmia and proteinuria. Analysis of these tests indicated that the greatest deviation from normal occurred during the early months of hospital stay when roentgenographic involvement was most marked.

Since this recently described disorder poses a diagnostic challenge to physicians, it is probable that other cases will be discovered in increasing number. The authors feel that retrospective analysis of pathological material from undiagnosed pulmonary cases of former years may be able, in some instances, to demonstrate the distinctive pathological features of proteinosis.

S. J. SHANE

Right Bundle-Branch Block. A Vectorcardiographic and Electrocardiographic study of Ventricular Septal Defect Following Open-Heart Surgery.

J. DICKENS, V. MARANHAO AND H. GOLDBERG: *Circulation*, 20: 201, 1959.

Seven patients who underwent open-heart surgery for repair of ventricular septal defect and in whom traumatic right bundle-branch block had been produced by the operative procedure, were studied by electrocardiograms and vectorcardiograms before and after operation.

In this study the differentiation between right ventricular hypertrophy, right bundle-branch block, and a normal variant could not be made electrocardiographically in the presence of an RSR pattern in V_1. However, after the production of right bundle-branch block by surgery characteristic changes in the vectorcardiograms were recorded in all patients.

The authors consider that these vector loop features may be applied in the differentiation between right bundle-branch block and right ventricular hypertrophy in the presence of an equivocal electrocardiogram.

S. J. SHANE

The Superiority of Enzyme Impregnated Paper for Determining Glycosuria in Patients Receiving Antituberculosis Drug Therapy.

R. W. PHILLIPS: *Dis. Chest*, 36: 160, 1959.

False-positive tests for glycosuria using Benedict's test were found in 30 to 40 patients receiving antituberculosis drug therapy with isoniazid, para-aminosalicylic acid and streptomycin, in a range of trace to two plus. None of the patients had a false-positive reaction for glycosuria when a specific enzyme-impregnated test paper was used.

The use of enzyme-impregnated testing paper is recommended for the routine determination of glycosuria in patients receiving today's commonly used antituberculosis drugs. It appears sufficiently accurate in detecting true glycosuria when compared with Benedict's reagent in testing urines with known concentrations of glucose.

S. J. SHANE

Prevalence of Pneumococcal Types and the Continuing Importance of Pneumococcal Infection.

R. AUSTRIAN: *Am. J. M. Sc.*, 238: 133, 1959.

This paper presents data relating to the isolation of pneumococci from patients on a general medical ward service for the five-year period, 1952-1957. In all, pneumococci were recovered from 1322 patients, of whom approximately two-thirds had pneumonia. Of the strains isolated, 48.8% were included in capsular types I to VIII inclusive and two-thirds of 209 pneumococcal bacteræmias were caused by organisms of the same capsular types.

The observations reflect the continuing importance of the pneumococcus as a cause of disease in man. In the opinion of the author they point also to a need for the reintroduction of capsular-typing serum and of satisfactory laboratory techniques for the isolation and identification of pneumococci if an accurate understanding of the causes of pneumonia is to be realized.

S. J. SHANE

SURGERY

Etiologic Factors in Polyposis and Carcinoma of the Colon.

J. E. DUNPHY, W. B. PATTERSON AND M. A. LEGG: *Ann. Surg.*, 150: 488, 1959.

Several cases are quoted of regression of carcinoma of the colon and rectum after proximal colostomy. Decrease in the number and size of rectal polyps after resection of the colon and ileo-rectal anastomosis has been observed fairly frequently. There is some evidence that preoperative irradiation may favourably affect the five-year salvage in carcinoma of the rectum. Other evidence is submitted which suggests that there may be a factor which leads to polyposis and carcinogenesis produced by the mucosa of the colon or activated by it, and which is removed or inactivated by diversion of the fæcal stream and partial colectomy. It is suggested that diversion of the fæcal stream may have a specific anti-tumour effect, so as to be of value in preparing the bowel for cancer surgery. It may be that the more frequent occurrence of carcinomatous implantation at the suture line may be due to improved preoperative preparation and elimination of preliminary colostomy. Further study of the effects of preliminary colostomy and preoperative irradiation is indicated, to try to show whether or not these methods lessen the dissemination of cancer at the time of operation.

BURNS PLEWES

Absorption of Surgical Catgut.

P. LAWRIE, G. E. ANGUS AND A. J. M. REESE: *Brit. J. Surg.*, 46: 638, 1959.

Great variation in the rate of absorption of various brands of both plain and chromic catgut has been recognized. The authors made experimental implants of these sutures into the lumbar muscles of rats, testing them at different intervals of time for strength and examining sections under the microscope. The inflammatory reaction, polymorphonuclear infiltration, fragmentation of the catgut, contraction of the abscess, formation of granulation tissue with giant cells and so on, are found to vary in degree and duration with the brand and the label. The early sterile pyogenic reaction around plain catgut results in such loss of strength that it is unreliable as a suture material for longer than two days. Medium chromic catgut always retains adequate strength long enough for firm union of wound edges in the absence of infection. BURNS PLEWES

Surgery in Pulmonary Tuberculosis.

R. S. MITCHELL AND O. AUERBACH: *Am. Rev. Respiratory Dis.*, 80: 207, 1959.

In tuberculosis therapy the goal should be a healthy patient who is not able or is unlikely to infect those in his environment. Attempts should be made to eradicate tuberculosis from the lungs, but not necessarily surgically, since it is obviously impossible to remove every tuberculous focus in the lungs. The persistent opinion of some observers that, in persons who are no longer infectious and who are receiving good chemotherapy, resection is indicated in the larger closed tuberculous lesions, especially those which were previously cavitary, should, in the opinion of the writers, be re-examined. The present widely held view that "open" lesions should be surgically resected or collapsed in persons who are otherwise well and non-infectious for many months during effective chemotherapy should also be re-examined, and the generally accepted policy of postponing surgery in most cases for six to eight months or until maximal improvement has been attained from antimicrobial therapy carefully scrutinized. The greater part of our attention should be concentrated on the treatment and prevention of chemotherapy failures, i.e. those persons who remain infectious and particularly those whose strains of tubercle bacilli have become predominantly drug-resistant. S. J. SHANE

Postoperative (Adynamic) Ileus. Its Prevention by Ambenonium Chloride.

C. BILBAO *et al.*: *Surgery*, 46: 1043, 1959.

On the basis of 400 surgical cases involving the abdominal cavity, the authors feel that prophylactic injections of ambenonium chloride are justified in the postoperative period. Each patient received injections every four hours, and an average of 19 injections each. The dubious advantage of receiving the drug by injection is believed to offset the undesirable effects of a gastric or intestinal tube.

[The authors state that it is accepted that a prophylactic treatment is always more effective and requires less medical attention than a therapeutic one. It is this type of thinking that has led to the promiscuous overuse of antibiotics. Our aim in surgery should be that of Doyen, to "suppress every manœuvre and every device which is not absolutely indispensable." This should also apply to the use of drugs such as the one under discussion.] T. A. MCLENNAN

THERAPEUTICS

Should Patients with Acute Streptococcal Tonsillitis be Treated with Penicillin?

H. DENNIG AND S. SCHMID: *Deutsche med. Wchnschr.*, 84: 1926, 1959.

Streptococcal tonsillitis with its typical white stippling of inflamed and greatly enlarged tonsils has to be distinguished from the more generalized form of pharyngitis, usually due to virus infection. It is in the former that penicillin unquestionably shortens the length of illness by at least one day. While this in itself is desirable, the more important value of penicillin is in the prevention of the late complications of streptococcal sore throat: rheumatic fever and acute glomerulonephritis. German medical opinion is by and large not favourably inclined to preventive treatment as practised in America and Britain. As there are no German studies relating to this problem, the authors recommend that the American results be adopted and the uniform method of treatment, as practised in the United States, introduced into German medical centres. Treatment should not limit itself to one single intramuscular injection of penicillin but should aim at a therapeutic penicillin level for at least ten days after the onset of disease. Thus, streptococci will be eliminated for at least several weeks and prevention of rheumatic fever and glomerulonephritis ensured. W. GROBIN

Clinical Trials of Phenethyldiguanide in Selected Patients.

R. E. TRANQUADA, C. R. KLEEMAN AND J. BROWN: *Am. J. M. Sc.*, 238: 187, 1959.

Results of oral treatment of selected diabetic patients with phenethyldiguanide (DBI) are presented. Twelve patients with labile diabetes were treated, three having a successful response to DBI and lowered insulin dosage. Four of eight patients with diabetes secondary to pancreatitis or pancreatectomy were controlled on DBI alone. Four of 10 patients on high insulin dosage (50 to 100 units per day) were controlled on DBI alone. One of four tolbutamide failures was successfully controlled on DBI. A high incidence of intolerable side effects was noted.

It is felt that DBI will be less useful in the therapy of stable adult diabetes because of the frequency of side effects, e.g. exacerbation of angina pectoris, and that its best application may lie in the stabilization of labile diabetes, the regulation of some patients with high insulin requirement, and the management of diabetics physically unable to give themselves injections. S. J. SHANE

ORTHOPÆDICS

Dislocations of the Shoulder with Special Reference to Accompanying Small Fractures.

R. H. HALL, F. ISAAC AND C. BOOTH: *J. Bone & Joint Surg.*, 41-A: 489, 1959.

Defects of the head and neck of the humerus related to a dislocated shoulder are frequently overlooked because they are not demonstrated on conventional routine roentgenograms and are not readily exposed by the usual anterior surgical approaches. The larger the defect in the humeral head, the more readily redislocation can occur. It is for this reason that a proper preoperative radiological evaluation is necessary.

Although a Putti-Platt, Matti, Magnuson, or comparable soft tissue capsulorrhaphy may be adequate in some patients, the more elaborate glenoidal repair of Bankart, Moseley or Gallie should be applied in cases

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of damaged meniscus or fractured glenoidal margin. When a large notch is demonstrable on the anatomical neck, posteriorly, the authors advocate a diametrically opposite capsular repair on the back of the humeral head, reattaching the capsule to the articular margin of the humerus to fill the defect and to give a smooth chondrosynovial surface.

A description of the "notch view" technique is given, which demonstrates in profile the postero-superior and antero-inferior regions of the articular surface and anatomical neck of the humerus. In essence this consists of having the patient lie on the fracture table in the supine position with his hand on the top of his head. The long axis of the shaft of the humerus must lie in the sagittal plane of the body, with the shoulder flexed slightly beyond 90°. The x-ray tube is tilted 10° toward the head of the table, with the beam centred on the coracoid process. In this technique, the uninjured anatomical neck appears as a fairly symmetrical V- or U-shaped groove with a smooth contour. This symmetry is usually lost, or smooth contour roughened by injury. The authors were able to demonstrate a posterior defect in the humeral head in 18 of 20 patients with recurrent anterior dislocation confirmed at surgery.

A tangential infero-superior projection of the glenoid should also be taken to demonstrate possible marginal fractures. ALLAN M. DAVIDSON

Factors Preventing Downward Dislocation of the Adducted Shoulder Joint.

J. V. BASMAJIAN AND F. J. BAZANT: *J. Bone & Joint Surg.*, 41-A: 1182, 1959.

This is a report on the electromyographic and morphological studies to determine the part played by various muscles during movement of the shoulder. Multiple concentric needle electrode were inserted into the relevant muscles of 22 young male volunteers. By means of six separate amplifiers and cathode-ray oscilloscopes, whose faces could be photographed simultaneously, even the slightest activity was accurately recorded. Various aspects were considered, but this paper deals primarily with activity in the case of (a) the static unloaded hanging arm and (b) the static loaded hanging arm. From detailed dissections of the rotator cuff mechanism, it became apparent that once the muscles and tendons were dissected from the capsule of the shoulder joint the capsule was quite lax except when the joint was well adducted. In this position, with normal anatomical relation of the scapula the head could not be moved downward. It was demonstrated that the superior part of the capsule of the joint and the associated supraspinatus tighten when the humeral head is pulled downward on the slope of the glenoid fossa.

The electromyographic recordings confirmed the findings of these dissections and thus reveal that it is not the vertical muscles such as the deltoid, biceps and triceps, that are primarily responsible for supporting the gleno-humeral joint. The explanation is that the normal obliquity of the glenoid is aided by the pull of the horizontal muscles. This in turn is of course dependent on the proper orientation of the scapula.

It would appear that the coracohumeral ligament is very important in this respect. In some persons it is well developed and undoubtedly plays a role in resisting downward pull. The supraspinatus comes into action to varying degrees depending on development of this ligament and the load.

It is apparent that this protective mechanism cannot be activated where there is abduction of the humerus. Tendency to subluxate inferiorly is also accentuated if the relative obliquity of the glenoid fossa and scapula is changed, as can happen in the case of the anæsthetized patient. ALLAN M. DAVIDSON

DERMATOLOGY

Disturbances of Pigmentation with Chloroquine.

J. L. C. DALL AND J. A. KEANE: *Brit. M. J.*, 1: 1387, 1959.

Three cases under treatment with chloroquine diphosphate—two of rheumatoid arthritis and one of disseminated lupus erythematosus—presented similar toxic reactions which included visual upset and bleaching of the hair and occurred at similar stages in treatment. Two of the cases also had undue erythema of the skin on exposure to sunlight.

Chloroquine may interfere with the deposition of pigment or replace normal pigment, and such changes appear to be reversible. ROBERT JACKSON

INDUSTRIAL MEDICINE

Mortality in City Firemen. II. A Study of Mortality in Firemen of a City Fire Department.

E. MASTROMATTEO: *A.M.A. Arch. Indust. Health*, 20: 227, 1959.

For the period 1921 to 1953, a study was undertaken to find out whether firemen, when compared with other men of similar age groups, had any difference in mortality, particularly from cardiovascular and respiratory causes, tuberculosis, and accidents and violence. Comparison of deaths from certain causes was made with those expected, using Ontario death rates for men of similar age groups and for the same period. On account of known mortality differences in urban and rural residence, further comparison was made with city men of similar age groups for the period 1937 to 1953.

The comparison revealed a highly significant excess in deaths from cardiovascular-renal diseases, a reduction from respiratory diseases and tuberculosis, and no significant difference from cancer, violence and accidents, digestive and genito-urinary diseases, or from all other causes. The comparison with city men confirmed the excess of cardiovascular-renal deaths. It showed also an excess from all causes together. A reduction was found in the deaths from tuberculosis, and no difference in the observed deaths from cancer, violence and accidents, and respiratory diseases.

The author discusses possible explanations for the differences under the following: statistical bias, chance variation, occupational factors, selection factors, non-occupational factors, and combination of factors. In his opinion the excess of cardiovascular-renal deaths is best explained by a combination of factors including selection of certain physical types for this work, increase in overweight in this group, lack of regular physical activity, and occupational factors that impose strain on the cardiovascular system. The latter do not actually cause the disease but may aggravate it. The reduction in deaths from tuberculosis and from respiratory diseases may be explained on the basis of careful medical selection and close medical supervision of city firemen. MARGARET H. WILTON

BOOK REVIEWS

BRONCHIAL ASTHMA, A SYMPOSIUM. Report of a meeting held on February 25, 1959, at the Royal Society of Medicine, London, England. 96 pp., Illust. The Chest and Heart Association, London, 1959. $2.00 approx.

This work is contained in a paperback book, and presents the discussion by a group of experts under the chairmanship of Sir Geoffrey Marshall, president of the Royal Society of Medicine.

For so small a volume, it is remarkably complete, dealing with every facet of the subject. Particularly interesting is the use of breathing exercises as physiotherapy. The use of steroids is not neglected.

This booklet is recommended reading for all physicians.

A BIBLIOGRAPHY OF INTERNAL MEDICINE. COMMUNICABLE DISEASES. Arthur L. Bloomfield. 560 pp. The University of Chicago Press, Chicago; The University of Toronto Press, Toronto, 1958. $10.00.

The author rightly believes that a knowledge of the historical development of a subject from its earliest inception, through its growth by the contributions of successive workers up to its present status, is essential to a proper understanding of that subject. He is also aware that the field of communicable diseases is very wide, and that the original articles dealing with it are so numerous and scattered that it would be impossible, except perhaps for a narrow specialist, to see them all.

This work is a successful effort to bring to the clinician and general reader, in readable form, a compilation of the significant contributions which have been made through the years to our knowledge of the communicable diseases—bacterial, parasitic and viral. To achieve his object the author has, of necessity, been rigorously selective. Only articles of real significance, in the light of present knowledge, have been included; those merely repetitive and those leading in wrong directions have been excluded. The original articles, with their references, are summarized and commented upon in a very pleasing style.

For the research worker in a narrow field this bibliography is quite inadequate; there are many more omissions than inclusions. For those with the broader interest indicated by the title it is a very interesting and informative work, and can be highly recommended.

EPIDEMIC DISEASES. The causes, course, and effects of the virus and bacterial diseases that have ravaged mankind, from the Black Death to the polio and influenza of today. A. H. Gale. 159 pp. Illust. Penguin Books, Harmondsworth, Middlesex, England, 1959. $0.70.

The excellence of the series of Pelican Books dealing with medical subjects has been commented on in this Journal in the past. The present volume by a distinguished English epidemiologist is no exception to this rule. Dr. Gale, who died before his book was published, was a man whose chief professional interest was the epidemiology of the common infectious diseases. It might be thought that this would be a difficult subject to make clear and interesting to the layman, but Dr. Gale has achieved this difficult feat, and this little book is highly recommended as a most readable and entertaining survey of the history of epidemic diseases, with particular reference to the British Isles. The story of the plague in England is particularly well written and is supplemented by diagrams. The account of the outbreak of plague in the little village of Eyam up in the Peak District where 259 inhabitants died of the plague between September 1665 and October 1666, leaving 33 alive, is as thrilling to read as a novel. The epidemic was fought by the rector who isolated the village from all surrounding contacts during this tragic period.

After a description of all the classical infectious diseases, Dr. Gale ends with an interesting survey of the relative importance of the different diseases in Britain at different times.

METABOLIC CARE OF THE SURGICAL PATIENT. Francis D. Moore, Moseley Professor of Surgery, Harvard Medical School, Boston. 1011 pp. Illust. W. B. Saunders Company, Philadelphia and London, 1959. $20.00.

In his introductory remarks the author has pointed out that his motives in writing this volume have been to bring together an area of knowledge which has grown up in the previous 15 years and, as well, to provide data that will be of help to the surgeon in the daily care of his patients.

This cannot be considered a textbook of surgery. Rather it points out that a balance between clinical judgment, operative skill and metabolic wisdom is essential in the management of a patient suffering from a surgical condition. A detailed study of all the various aspects of metabolism in the patient is given as a base-line, and then the variations which are found in those who have been operated on or suffered trauma, and the changes which occur in convalescence, are presented. The various aspects of surgical endocrinology in metabolism are dealt with at length. The final chapter is devoted to early feeding and its effects on nitrogen balance and wound healing.

Dr. Moore in his book has made a monumental contribution to our knowledge and understanding of what to expect in the normal postoperative course of surgical patients, and also the complicated course. This book should be available to every surgeon so that he may, by reference to it, gain a clearer insight into the usual and unusual patterns of metabolic activity in surgical patients.

KILOCURIE COBALT 60 THERAPY AT THE RADIUMHEMMET. Equipment, Technique and Dose Measurements. Acta Radiologica, Supplementum 179. S. Hultberg and others. 286 pp. Illust. Acta Radiologica, Stockholm, 1959. $6.30.

This volume contains very valuable basic information on the design, construction, auxiliary devices and physical data connected with the Siemens Gammatron I, a kilocurie cobalt 60 unit (AECL source) built to specifications of the physicists and therapists at Radiumhemmet. The equipment was ready for use in April 1957. More than half of the volume is taken up with charts of measured isodoses, including stationary fields (FSD 40 to 100 cm.), wedge fields, and rotational distributions (less than 360°). A very large amount of work has gone into this volume, chiefly of interest to medical radiation physicists, but also instructive as to the care and preparation necessary in accurate telecobalt-therapy. A second, more clinical volume is planned for a date when case load and follow-up are suitable.

(Continued on advertising page 22)

QUALIFIED PATHOLOGIST as director of clinic pathology services for two hospitals in Ontario's Niagara Peninsula. Completely modern and up to date base laboratory with well-qualified technicians. Second hospital within twenty miles. Attractive financially to a doctor who will develop services. Apply to Administrator, Port Colborne General Hospital, Port Colborne, Ontario.

PARTNER REQUIRED for general practice in east-central Alberta before July 30, 1960. New medical building completed 1959, 25-bed hospital under construction, ready for occupancy this year. Equal partnership in reasonable time if mutually satisfactory. Reply, stating qualifications, age, marital status, religion, and references to Dr. J. C. O'Brien, Coronation, Alberta.

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PHYSICIAN FOR AREA CHEST CLINICS, investigation and and treatment unit. Mobile Van in operation. Some duties in geriatric division. Self-contained apartment available if desired. Apply stating experience and salary desired to Medical Superintendent, Freeport Sanatorium, Kitchener, Ont.

WANTED.—Well-trained general practitioner (2 years' rotating internship preferred) for southern Ontario clinic. Reply stating age, race and salary expected to Box 660, CMA Journal, 150 St. George St., Toronto 5, Ont.

WANTED.—CANADIAN GRADUATE as assistant in general practice with eventual partnership. Western Ontario town with excellent hospital facilities. Reply stating age, qualifications and salary expected to Box 664, CMA Journal, 150 St. George St., Toronto 5, Ont.

ASSISTANT, with view to partnership within six months, required by general practitioner in Manitoba. The vacancy has been created due to retirement of senior practitioner. The group practice will eventually consist of three partners. The introductory period of assistantship carries a salary of $700 plus $50 car allowance. There is one other group practice in the town. Reply to Box 677, CMA Journal, 150 St. George St., Toronto 5, Ont.

ASSISTANT BACTERIOLOGIST. — THE HOSPITAL FOR SICK CHILDREN, TORONTO, CANADA. Applications are invited from medical graduates with training in bacteriology and some interest in pædiatrics. Initial appointment will be for a two-year trial period but subject to full appointment beyond this. Starting salary commensurate with training and experience. Applications with full personal details and names and addresses of three referees to be sent to the Director, Hospital for Sick Children, 555 University Avenue, Toronto 2, Ont.

OPENING FOR DOCTOR (late 20's, early 30's), in established general practice. Greater Vancouver area—excellent hospital facilities. Assistant-associateship; salary and car expenses. If interested write for further details and application form to Box 680, CMA Journal, 150 St. George St., Toronto 5, Ont.

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INTERNISTS.—One year appointments available in the Department of Internal Medicine, Cleveland Clinic. Excellent opening for practice time credit in junior staff position for those who have completed formal training programme. Apply.—Director of Education, Cleveland Clinic, 2020 East 93rd St., Cleveland 6, Ohio.

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THE COMMUNITY OF STRATHCLAIR, MANITOBA requires doctor for private practice. Services of 25-bed Shoal Lake Hospital available in 15-minute drive on paved #4 highway. Will build modern home and office, rent-free for 6 months, for accepted applicant. Lucrative district, in close proximity to Clear Lake National Park and good hunting and fishing facilities. Apply before 31 March 1960 to Mrs. W. Lee, District Doctor's Committee, Strathclair, Manitoba.

POSITION OPEN.—The Victoria Union and Holy Family Hospitals, Prince Albert, Saskatchewan, require the services of a certified pathologist to take complete charge of the laboratory department at both hospitals. Apply stating qualifications to: H. H. Bassett, Secretary, Board of Directors, Victoria Union Hospital, Prince Albert, Saskatchewan.

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ASSISTANT for July 1960 for two-man general practice clinic in Metropolitan Toronto. Opportunity for permanent association—partnership if mutually suitable. Reply to Box 648, CMA Journal, 150 St. George St., Toronto 5, Ont.

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HOUSE AND PRACTICE FOR SALE in a central Ontario town. Records, office equipment and introductions included. Owner wishing to specialize. Reply to Box 510, CMA Journal, 150 St. George St., Toronto 5, Ont.

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UNOPPOSED GENERAL PRACTICE in central Manitoba town of 700. Large surrounding area. Annual gross above average; overhead low; office situated in modern 19-bed hospital. Price $9500 includes three-bedroom house, equipment and records. Reasonable terms accepted. Reply to Box 668, CMA Journal, 150 St. George St., Toronto 5, Ont.

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WANTED.—House physicians, 345-bed general hospital, rotating service—$300 per month plus $50 for living out if married and $25 for living out if single. Foreign graduates must speak fluent English and have certificate from Educational Council. Apply immediately for early appointment. Kentucky Baptist Hospital, Louisville, Kentucky, H. L. Dobbs, Administrator.

ST. LUKE HOSPITAL, in Montreal, capacity 451 beds, is considering applications for internship or residency in the different services of a general hospital. The institution is approved with full accreditation by the Joint Commission on Accreditation of Hospitals. The Royal College of Physicians and Surgeons of Canada approves for advanced graduate training the following specialties: anæsthesia, general surgery, internal medicine, orthopædic surgery, otolaryngology, pathology, radiology (diagnostic) and radiology (therapeutic). Applicants may address their applications to Dr. H. I. Tetreault, Medical Superintendent.

PÆDIATRIC RESIDENCY available July 1, 1960, 2-year approved residency. 1st year stipend $3900, 2nd year $4200. Apply Arthur L. Tuuri, M.D., Chief of Pædiatrics, Hurley Hospital, Flint 2, Michigan.

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PATHOLOGY RESIDENCY.—Fully-approved for four years in P.A. and C.P. Four certified pathologists. 935 beds and bassinettes. Surgicals—14,802; autopsies—346; total exams—971,817. Indiana University teaching conferences and appointments available. Stipend first year $3336 with annual increases and opportunity for extra income. Housing on premises available. Indiana licensure is necessary. Apply to Dr. Lester H. Hoyt, Director of Clinical Laboratories, Methodist Hospital, Indianapolis 7, Indiana.

RESIDENCIES MEDICINE AND PÆDIATRICS.—Active 300-bed general hospital. Organized teaching programme with full-time board specialists. Salaries range from $315 to $415. Eligible California Licensure. Write: Director of Medical Education, Kalser Foundation Hospital, Oakland 11, California.

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Fellowships

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BOOK REVIEWS

(Continued from page 703)

ARTHRITIS. Medical Treatment and Home Care. John H. Bland. 208 pp. Illust. The Macmillan Company, New York; Brett-Macmillan Ltd., Galt, Ont., 1960. $4.95.

In his preface to this volume the author states that "It is impossible for the best and most communicative physicians to tell even the bare outlines of the arthritis story to all patients; this book is written to fill that need." Dr. Bland, who is well qualified for this assignment by his training, experience and sympathetic understanding, has accomplished it admirably.

Every physician who cares for patients suffering from rheumatoid arthritis or osteoarthritis will realize that successful treatment of these chronic, frequently discouraging and disabling diseases depends in large part on the patient's motivation and the persistence with which he follows, throughout the course of his illness, certain all-important fundamentals of home care. Such motivation requires a reasonable understanding of the nature of the disease, the course it may follow, and the rationale of common-sense measures which facilitate natural recovery, relieve discomfort, prevent disabling deformities, improve function, conquer physical handicaps and restore useful, independent living. Lacking this knowledge and fearing the unknown, the uninformed arthritic

(Continued on page 26)

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1. FORD, RALPH V. The clinical pharmacological investigation of a new benzothiadiazine diuretic, CMR-807 (Naqua). To be published.
2. HUTCHEON, DUNCAN E. The diuretic action of NAQUA (CMR-807) in patients with congestive heart failure. To be published.

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BOOK REVIEWS

(Continued from page 22)

sufferer is incapable of establishing realistic objectives, fails to grasp the importance of faithful adherence to simple and undramatic treatment principles, and is prone to attitudes of despair and defeatism, or in his desperate grasping for the straw of a rapid, sure-fire "cure" falls helpless prey to quacks or faddists. The comments in this volume on fads, fancies, common misconceptions and worthless "remedies" provide valuable reading for even the most intelligent patient. The techniques of useful home-treatment measures and their mode of action are described in painstaking but simple detail.

Together with the handbooks on rheumatoid arthritis and osteoarthritis published by the Canadian Arthritis and Rheumatism Society, this book is an important and highly recommended source of information for patients with these diseases, for their families and their physicians.

HEADACHE — DIAGNOSIS AND TREATMENT. Arnold P. Friedman and H. Houston Merritt. 401 pp. Illust. F. A. Davis Company, Philadelphia; The Ryerson Press, Toronto, 1959. $8.75.

Twelve different men have contributed to this book on one of the commonest symptoms of human discomfort, namely, headache. In spite of the multitude of authors, there is a minimum of repetition. Each author emphasizes the importance of the various concepts of headache in his own field, and each chapter is well written and well organized.

There are chapters on the mechanisms by which headache is produced, with examples of specific disease entities falling under each of the mechanisms: discussion of the various eye, ear, nose and throat conditions as a source of headache, of the debatable role of allergy in the production of headache, and of the systemic diseases in which headache is present and the mechanisms involved in its production.

The choice of drugs is thoroughly dealt with, with indications for their use, dosages, duration of treatment, actions, side effects and contraindications. Clinical features and therapy of headache in various intracranial disorders, cranial neuralgias, and the surgical treatment of headache are well summarized. Excellently covered are the guiding points in taking the history of headache, as well as the mechanical and pharmacological tests employed.

Particularly thought-provoking are the chapters on migraine, tension headache, and psychogenic headache, discussing symptoms, differential diagnosis, and symptomatic and prophylactic treatment, with a general review of current psychiatric conceptions about each, and the role that the family physician can play in treatment. This is an informative and stimulating book, well worth reading.

DIE ABNUETZUNGSERKRANKUNGEN DER SEHNEN UND IHRE THERAPIE (Degenerative Diseases of Tendons and their Treatment). Doz. Dr. H. Schneider. 202 pp. Illust. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1959. DM 36.-

In the introductory part of this book the author presents a very interesting review of the subject. His statements are supported by personal observation, research and sufficient references to the literature. The following is an outline of the scope of this book.

Only lately has it been shown that degenerative diseases in the tendons and their insertions may start as early as the third decade of life. The changes are gradual and barely noticed at first, but as time goes on pain and disability increase. Histological examination has proved that so-called periarthritis, coracoiditis, epicondylitis, etc., are actually diseases of tendons. The tendons are not attached to periosteum but to the bone, and in the region of insertion there is no periosteum. This should have been known since 1922, when the German anatomist Weidenreich first published his work on this subject. The fact that none of the degenerative diseases of the tendons are deadly is the reason why the practical importance of this discovery was not appreciated for decades.

Degenerative diseases in tendons are caused in a great number of cases by continuous or repeated use (overuse, as in industry) or sudden overactivity (overuse, as in sports). This is a fact recognized by the new German state where "chronic diseases of tendon and muscle insertions—through overuse" are recognized as industrial diseases.

Another cause for degenerative disease lies in the fact that most of them are anchored to a bony prominence which is usually superficial and easily exposed to trauma.

Tendon diseases are common and therefore besides their medical importance their impact on production in industry and on economy has to be considered.

The book is divided into general and special parts, the first presenting anatomical and histological details with etiology and pathogenesis, and the second describing the different regions where diseases occur.

This is a comparatively small book, carefully written by an obviously experienced author, full of food for thought and practical advice on treatment.

CUTANEOUS MANIFESTATIONS OF THE MALIGNANT LYMPHOMAS. S. M. Bluefarb. 534 pp. Illust. Charles C Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1959. $17.00.

Two very extensive chapters on mycosis fungoides and Hodgkin's disease, and a shorter study of lymphosarcomas (including leuko-

sarcoma) are included in this volume. Although the title mentions only the cutaneous manifestations of the above entities, there is a very complete review of their etiology, pathology, clinical aspects, prognosis and treatment. In each chapter many clinical case reports are reviewed, and indeed one is somewhat overwhelmed by their numbers; one wonders whether the multiplicity of individual cases adds anything to the clearer understanding of conditions with such wide variations of clinical manifestations.

The "tumeur d'emblée" type of mycosis fungoides is, according to the author, a manifestation of lymphosarcoma; the "erythroderma" form is either lymphocytic leukæmia, Hodgkin's disease or reticulum cell lymphosarcoma. He emphasizes the point that in many instances the cutaneous manifestations are the first discernible sign of the disease, which thus permit the diagnosis before changes in other organs are apparent.

The presentation of the book is excellent and there are many good photographs of clinical features, pathological specimens and slides. At the end of each chapter there is a very impressive and complete list of references. The monograph is concluded by a short description of the immunological status of the malignant lymphomas. Dermatologists, internists, and those interested in lymphomas will find a great amount of information in this volume, which will be a valuable addition to any reference library.

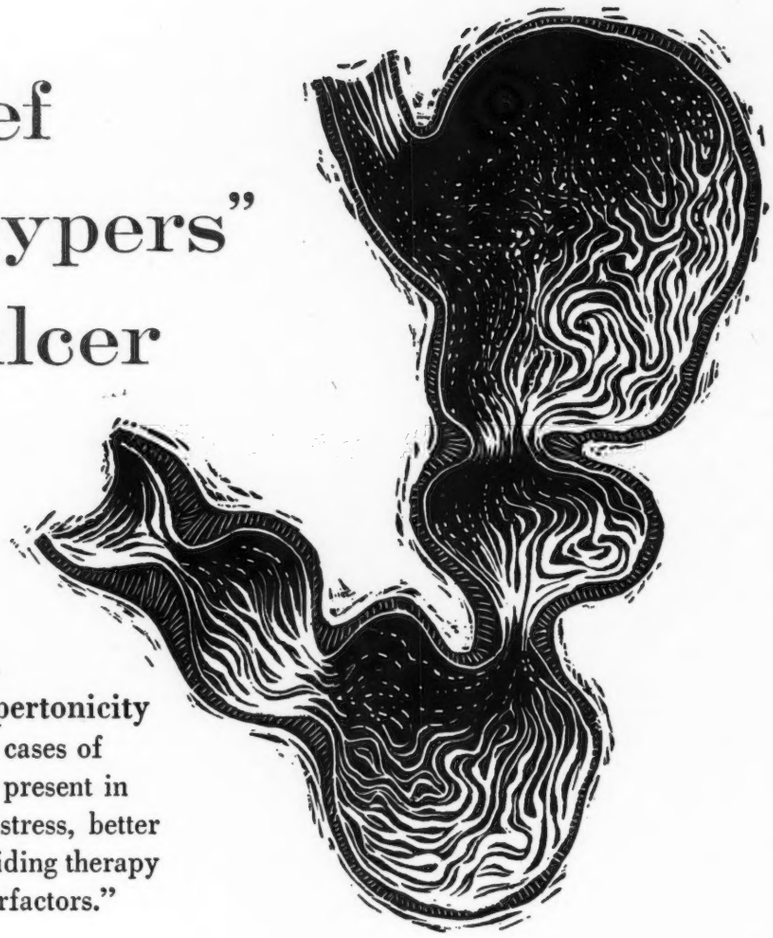
A SYSTEM OF ORTHOPÆDICS AND FRACTURES. A. Graham Apley, Consultant Orthopædic Surgeon, the Rowley Bristow Orthopædic Hospital, Pyrford, Surrey, England. 357 pp. Butterworth & Company Limited, London, 1959. $9.50 (interleaved edition $13.50).

As the author explains in his preface, this book is based on the notes of the review courses given at the Rowley Bristow Orthopædic Hospital for F.R.C.S. candidates. It is devoid of illustrations, and of course makes no effort to be an authoritative textbook in the usual sense of the word. The book is divided into three parts: general orthopædics, regional orthopædics, and fractures and dislocations. The "system" which guides the examination of each entity is governed by the three commandments: look, feel, move. In this way, current orthopædic thought is admirably and concisely summarized. In fact, no topic appears to have been left out, and there are just the right number of "pearls" required for examination-passing purposes.

The author maintains the typical British scepticism towards the value of end-bearing amputations, and mentions that hip disarticulations are very difficult to fit. Apart from these contradictions of Canadian experience, there are very few criticisms indeed that can be made of his statements.

This book is decidedly a worthwhile investment for anyone taking advanced training or preparing for senior qualifying examinations. In view of this, and the gospel-like nature of the volume, it is regrettable that its size is just too big for at least the average Canadian pocket. The author and the publisher would be well advised to print the next edition on rice paper of approximately hymn-book size so that it could be carried around more easily.

Better relief from the "hypers" in gastric ulcer



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References: 1. Morrison, S.: Am. J. Gastroenterol. *22*:301 (1954). 2. Kastner, J. W.: Anca Laboratories. 3. Cahen, R. L., and Tvede, K.: J. Pharmacol. & Exper. Therap. *105*:166 (1952). 4. Berger, A. R., and Ballinger, J.: Am. J. M. Sc. *214*:156 (1947). 5. Sollman, T.: Manual Pharm., Saunders, Philadelphia, 1957, p. 936. 6. Dripps, R. D.: J.A.M.A. *139*:148 (1949). 7. Fierst, S. M.: in Current Therapy, Saunders, Philadelphia, 1958, p. 237.

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